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**In a context of digital (r)evolution and
hyperconnectivity, where is innovation in healthcare?
Who are the players? And how can a company be
innovative within an R&D center?**

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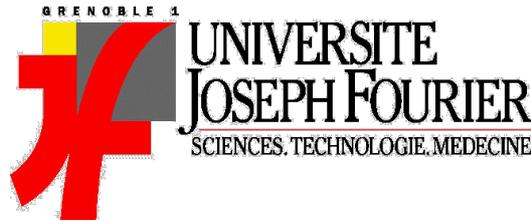
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In a context of digital (r)evolution and hyperconnectivity, where is innovation in healthcare?



Faculté de pharmacie de Grenoble

Année 2015

Dans un contexte de (r)évolution numérique et d'hyperconnectivité, où sont les innovations en santé ?
Qui en sont les acteurs ? Et comment une compagnie peut être innovante au sein d'un centre R&D ?

THÈSE

PRÉSENTÉE POUR L'OBTENTION DU TITRE DE DOCTEUR EN PHARMACIE

Jérôme Topsent

[Données à caractère personnel]

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Abbreviation

ADSC: Adipocyte Derived Stem Cell

AE: Adverse Events

ATMP: Advanced Therapy Medicinal Products

CHS: Community Health Care System

CSI: Competitive and Scientific Intelligence

CT: Cell Therapy

DNA: Desoxyribo Nucleotide Acid

H2IS: Hospital Health Information System

HIV: Human Immunodeficiency Virus

HHS: Home healthcare system

IoT: Internet of Thing

iPS: Induced Pluripotent Stem cell

IT: Information Technology

KOL: Key Opinion Leader

mAb: Monoclonal Antibody

MD: Medical Device

OCDE: Organisation de Coopération et de Développement Économiques

PCR: Polymerase Chain Reaction

QR Code: Quick Response Code

R&D: Research and development

RID: Research, Innovation and Development

RFID: Radio Frequency Identification

Rx: Treatment under prescription

SHIELD: Skin Health Investigation Education and Longevity Development

WHO: World Health Organization

XSCID: X linked Severe Combined Immune Deficiency

WD: Wearable device

Résumé

Le monde d'aujourd'hui change de manière drastique, dans tous les secteurs nous voyons des innovations apparaître, ceci étant guidé par l'évolution des moyens de communication et la révolution numérique en marche. Le monde de la santé n'en est pas épargné. Plusieurs innovations peuvent être citées : De l'avènement des médicaments biologiques aux nouveaux dispositifs médicaux en passant par le développement de technologies support tel que les nanotechnologies et biotechnologies. C'est la manière de soigner qui en est bouleversée, la médecine tend à devenir préventive plutôt que curative, les stratégies deviennent plus personnalisées. Tout cela pour répondre à une évolution des besoins de santé (chronicisation des maladies, vieillissement de la population...).

De plus, les compagnies pharmaceutiques cherchent aussi à être plus innovantes au sein de leur R&D. En effet, les systèmes cloisonnés de R&D classiques sont arrivés à leurs limites. Afin de comprendre ce nouvel environnement, un processus de recherche d'innovation a été implémenté au sein d'une entreprise pharmaceutique. Ce processus se décompose en trois parties : Trouver, analyser et suivre l'innovation.

Pour ce faire, plusieurs chemins ont été essayés. Tout d'abord la recherche d'innovation ayant commencé par la consultation de newsletter et de sites dans divers domaines (ce qu'on appellera de la recherche passive) a vite dérivé vers l'échange entre les personnes et la création d'un réseau au sein de l'entreprise. Ainsi les besoins de l'entreprise sont mieux identifiés et la recherche d'innovation est orientée (ce qui est assimilé à de la recherche active)

Ensuite une analyse a été nécessaire pour chaque innovation, pour ce faire différents outils ont été utilisés (Orbit, Pharmaproject, Pub Med, Clinicaltrial.gov, site de compagnies) afin de dresser un paysage des tendances et de la compétition.

Une fois ceci effectué, les innovations ont été présentées à un groupe d'experts pour juger de leur pertinence. Puis ces idées ont été téléchargées sur un site, créé pour cette mission, afin d'être partagé à l'ensemble des collaborateurs.

Cette mission a permis de montrer l'importance du besoin de communication et de création d'un réseau afin de faire, de manière collective, une recherche et un suivi de l'innovation. La recherche d'innovation ne peut être un processus supporté par une personne. Ce qui est d'autant plus vrai étant donné la quantité d'information disponible sur internet.

En conclusion, ce qui a été fait :

- Un processus entier a été imaginé et mis en place
- Les recherches actives ont été préférées aux passives
- 6 opportunités ont traversé tout le processus, ces innovations semblent pertinentes pour la compagnie
- Grâce au réseau créé, trois analyses ad-hoc ont été réalisées à la demande sur des innovations :
 - o Paysage sur les anticorps bispécifiques
 - o Paysage sur les patches liquides
 - o Paysage sur les innovations en emballage

Les recommandations sont :

- Qu'il faut développer la partie analytique et allouer plus de ressources (personne et matériel)
- Qu'il faut mettre en place un réseau durable entre les personnes de la compagnie
- Qu'il faut être un maximum proactif, c'est-à-dire être innovant plus que suiveur
- Qu'il est crucial de déterminer la direction à suivre, en effet beaucoup de technologies sont déjà disponibles il faut déterminer les applications.

Les perspectives sont :

- Il existe un paradoxe dans l'innovation, nous le monde est pour et pourtant l'innovation est lente : Les gens sont naturellement contre le changement
- Il est crucial d'identifier les conflits d'engagement afin de débloquent l'innovation
- L'innovation ne vient qu'avec des stratégies à long terme
- Il n'est jamais possible d'être sûr à 100% que l'innovation rencontrera le succès.

Mots clé : Innovation, Object Connectés, Biotechnologies, Nanotechnologies, Vaccination, Open Innovation, Dermatologie, Veille concurrentielle

Abstract

The world in which we live today is drastically changing in every field. Innovations come out, led by the evolution of our new communication capacities and the digital revolution. Healthcare is changing too. Many innovations can be listed: From the resurgence of biological medicine to the new medical devices, including the development of new supports technologies such as nanotechnology and biotechnology. Furthermore the way that we treat diseases is changing too. Tomorrow, medicine will tend to be more preventive than curative. Strategies are becoming more personalized and respond to the evolution of the health needs (diseases are becoming chronic and there is a global aging of the population).

Besides this, pharmaceutical companies try to be more innovative within their R&D centers. Indeed, closed system of classical R&D has reached its limits. With the aim of understanding this environment, a process of research of innovation was set and implemented within a dermatological company. This process is made up of three parts: Spot, analyze and follow innovation.

Therefore, several paths have been tested. First of all, innovation spotting began throughout scrutinizing industry newsletters and websites in a wide range of domains (It is what we have called passive search). Then we focused our energy on creating an exchange between people and a network within the company. Thus, the needs of the company were better identified and the innovation research was then oriented (This is the active search).

After spotting an innovation, an analysis was required. To this end, several tools were used (Orbit, Pharmaproject, Pub Med, Clinicaltrial.gov, company's website). Therefore, landscapes of trends and competition were performed.

Once this was done, innovations were presented to a team of experts to assess the relevance of each ones. Then ideas were uploaded on a platform, which was designed for the mission, with the aim of sharing them with every collaborator within the company.

This mission revealed the importance of the communication system within a company as much as the need to create a sustainable network. Therefore, in a collaborative way, spotting and watching innovation can be performed. Finding innovations is not a process that can be carried by a single person. This is even truer for the web research due to the increasing amount of data available on Internet.

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To conclude:

- A whole process has been set and implemented
- Active searches were preferred to passive ones
- Some parts of the process were eliminated because there were not enough resources to make them work
- 6 opportunities were finally presented after the process selection. Those innovations seem to be relevant for a dermatological company
- Three ad-hoc analysis were performed after a request from three different departments

Recommendations could be:

- To further develop the analytical process and needs, in line with resources allocations (both personnel and tools)
- To set a sustainable and integrated network with other players in the company dealing with the same issues
- To be proactive as much as possible, being real innovators more than followers
- To clearly determine the direction to follow: some available technologies may be new opportunities for several applications.

Perspectives are:

- The paradox of innovation: everybody loves it, however innovation is slow. People are naturally resilient to change.
- It is crucial to identify the conflict of commitment: we cannot be innovative naturally because it goes against commitment already set. Once it has been identified, it is easier to be innovative.
- Remember: innovation comes with a long-term strategy
- There is no certainty whether the innovation will work or not; would a good multifactorial analysis be able to anticipate it? (e.g., Google glasses and Apples iWatch have so far been failures)

Key words: Innovation, Internet of things, Biotechnology, nanotechnology, vaccination, open innovation, dermatology, Competitive intelligence

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Introduction

The world in which we live today is drastically changing. A new revolution is in progress. It is the revolution of digital¹ and hyperconnectivity². Today more than ever, people are connected but not only. The trend is for everything to be connected as well. Moreover new technologies are emerging, such as 3D printing that will impact widely lots of processes. To be focused on the pharmaceutical and medicinal issue, we can say that this revolution is changing the R&D process, manufacturing, clinical trial but also the relationship between health professionals and patients. So it is changing the whole healthcare process from the conception of a new drug candidate to the administration and the monitoring in the patient. Furthermore, all kind of resistance is useless because everyone will be impacted by the digital world sooner or later³.

This revolution is changing the healthcare system worldwide too. So the patient becomes the main actor in his health management⁴.

The Internet of thing (IoT) and wearable devices will enable the patient to self-monitor his health to prevent or stop most part of diseases. Therefore one doesn't have to wait until the sickness appears. Patient will also be able to reduce the cost of healthcare while doing, by himself or through home based telemedicine, a big part of his daily care. Those entire personal, wearable and ubiquitous devices will improve the healthcare⁵. IoT could also improve packaging by ensuring security and the use of the product. But it is not the only innovation met in packaging⁶. All this is possible because by manufacturing a big amount of technologies it decreases their production cost really fast. For the record, companies are developing a smart packaging which uses low-cost technology named Radio Frequency Identification (RFID)⁷.

Another aspect is the development of theragnostic⁸ which is the new way to treat people. Usually we develop drugs for specific diseases and give it to all patients bearing this pathology; this is called the blockbuster strategy. The thing is some people will be better responder than others. And the worst is that some will develop adverse effects more than others. To avoid this kind of hazardous issue, in other words to be sure that patient will be a good responder and to be more cost-effective in healthcare, theragnostic was developed. It is formed of four components:

- Biomarkers of the disease
- Companion diagnostic test which is associated to a treatment and which specifically recognizes these biomarkers
- A specific treatment for responder patient
- Wearable devices and internet of thing to monitor illness

With this strategy, patient will receive only a treatment that is working for his disease according to his specificities and his environment. It is the personalized medicine.

The way we produce drugs is also changing from chemical, little and easily produced entities to biological, big and complex molecules. Through biotechnology, advanced therapies but also nanotechnology and so on, a brand new arsenal of innovative therapies is available for treatments.

An overview of all those innovations in healthcare will be provided through this document, as well as an overview of all the actors involved. It is important to notice that presented innovations in

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healthcare are a part of something bigger; to be exhaustive is not the purpose. To provide an overview of what can be done as innovation in the field sounds more achievable.

Finally, the organization of pharmaceutical companies has changed these last decades. From lots of little companies, mergers and acquisitions have created big pharma companies. This provides them big R&D centers. However, those centers have a recurring problem, which is to improve the innovative aspects of their products⁹. Question is why? Why with more people involved in a project, more financial support and other advantages, the innovation process seems to lose steam? What are the solutions to improve this process? What are the difficulties met?

After a review concerning the needs of tomorrow's healthcare and innovations in the field (which we shortly summarized above), we will discuss about a strategy, among others, developed to improve innovation finding¹⁰. Then, a process implemented within a dermatological company to spot, analyze and follow innovation will be exposed and discussed.

Before all this, a short summary about the company where the internship took place is necessary.

In 1981, a joint venture, between Nestlé and L'Oréal, created a new pharmaceutical company called Galderma. Galderma's goal is to become a global leader in dermatology. The head office is situated in Lausanne (Switzerland). Mr. Humberto C. Antunes who is the head of this company, has more than 3000 collaborators and more than 5000 employees.

Galderma focuses on innovation with medical and aesthetic purposes. As a matter of fact, each year, twenty percent of the global revenue is invested in the R&D. Therefore, research and development within the company is at its peak performance. Furthermore it also has an international vocation. As a matter of fact, there are five centers located in Sophia Antipolis (France), Princeton (USA), Uppsala (Sweden), Egerkingen (Switzerland) and Tokyo (Japan). The three production's sites are situated in France, Canada and Brazil. Moreover, the company is present worldwide; affiliates can be found in 33 different countries. Its products are sold in more than 70 countries. Every year, the working capital turnover represents more than 1 billion Euros.

As Galderma invests in R&D, it can offer a wide line of medical solutions such as Différine®. This product was launched in 1995 to treat moderate acne. This product along with Oracea®, are part of the top 10 sales worldwide in dermatology. The portfolio of Galderma is continuously growing. Concerning therapeutic areas, Galderma focuses on rosacea, psoriasis, onychomycosis, pigmentation disorders, cutaneous cancer (excepted melanoma) or even more skin aging. Since a few years, a new line of products is also available in parapharmacies as a brand called Cetaphil®.

Last but not least; Galderma is now totally part of Nestlé, which bought the part of L'Oréal this year (2015). Galderma is now the Rx part of Nestlé Skin Care. A large number of reorganization are undergoing within the company. Nestlé Skin Care's vocation is to become the leader for dermatology innovation. Therefore, new centers are opening worldwide. To be even more accurate, 12 centers of Open Innovation, called Skin Health Investigation Education and Longevity Development (SHIELD). These centers apply new strategies of research and development such as open innovation or crowd sourcing. This is what has been tested during the internship. This paper is a thorough explanation of what we are going to deal with.

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Introduction (Français)

Le monde dans lequel nous vivons aujourd'hui change de manière drastique. Une nouvelle révolution est en marche. C'est la révolution du numérique¹ et de l'hyperconnectivité². Aujourd'hui, plus que jamais, les personnes sont connectées mais pas seulement. Tout tend à être connecté également. De plus, de nouvelles technologies sont en train d'émerger, comme l'impression 3D, et vont impacter largement plusieurs processus. Pour se centrer sur le monde médical et pharmaceutique, nous pouvons dire que la révolution change les processus classiques de R&D, la production, les études cliniques mais aussi la relations entre les professionnels de santé et le patient. Ainsi c'est tout le processus de santé, depuis la conception du médicament candidat jusqu'à l'administration et la surveillance du patient, qui change. En outre, toute résistance est inutile, tout le monde sera assimilé au monde numérique tôt ou tard³.

Cette révolution change les systèmes de santé à travers le monde également. Le patient devient l'acteur principal du management de sa santé⁴.

L'internet des objets et les dispositifs portables (à comprendre wearable devices) vont permettre au patient d'auto surveiller sa santé et ainsi prévenir voir arrêter la plupart des maladies. Ainsi n'importe qui n'aura plus à attendre que la maladie n'apparaisse. Le patient sera aussi capable de réduire le cout des soins de santé car il pourra faire, de part lui-même et au travers de la télémédecine, une grande partie de ses soins quotidiens. Et ce depuis chez lui. Tous ces dispositifs portables, ubiquitaires permettrons d'améliorer les services médicaux⁵.

L'internet des objets pourra aussi améliorer l'emballage en améliorant la sécurité et la bonne utilisation des produits. Mais ce ne sont pas les seules innovations rencontrées en emballage⁶. Tout ceci est possible car la production de masse de technologies va permettre une réduction de leur prix de fabrication et ce plus rapidement qu'on ne le pense. Pour informations, des compagnies sont déjà en train de développer des emballages intelligents qui utilisent des technologies à bas prix tel que les RFID (Radio Frequency Identification)⁷.

Une autre chose à prendre en compte est le développement de la théranostique⁸ qui est une nouvelle manière de traiter les gens. Usuellement, les médicaments étaient développés pour une maladie spécifique et donnée à tous les patients qui portaient cette pathologie. C'est une stratégie dite de « blockbuster ». Le problème étant que certaines personnes étaient meilleurs répondeurs que d'autres. Et pire, que certains développaient plus d'effets indésirables que d'autres. Pour empêcher ce genre de réaction dangereuse, en d'autres mots pour être sûr que le patient sera bon répondeur et ainsi diminuer le coût de santé, la théranostique a été développée. Cette stratégie s'articule autour de 4 piliers :

- Les bio-marqueurs de la pathologie
- Les diagnostics compagnons qui sont associés à un traitement et reconnaissent spécifiquement ces bio-marqueurs
- Un traitement spécifique pour les patient répondeurs
- Des dispositifs portables ainsi que l'internet des objets pour mieux surveiller l'évolution de la maladie

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Avec cette stratégie, le patient recevra seulement un traitement qui fonctionnera sur sa maladie en concordance avec ses spécificités et son environnement. C'est ce qu'on peut appeler de la médecine personnalisée.

La manière dont nous produisons les médicaments change également. De petites molécules chimiques, facilement produites et caractérisables, les industries développent des grosses molécules biologiques et complexes. Au travers de la biotechnologie, des thérapies innovantes mais aussi des nanotechnologies, un nouvel arsenal de thérapie est disponible pour les traitements. Un aperçu de ces innovations en santé sera exposé dans ce document, de même qu'un aperçu des acteurs impliqués. Il est important de noter que les innovations présentées en santé sont une partie de quelque chose de plus grand. Être exhaustif n'est pas possible. Donner un aperçu semble plus correcte.

Finalement, les organisations des compagnies pharmaceutiques ont changé depuis quelques décennies. De plusieurs petites compagnies, les fusions et acquisitions ont permis de créer d'en créer de plus grande et puissante. Ceci a permis de créer également de plus grand centre de R&D. Cependant, ces centres ont un problème majeur qui est qu'ils n'arrivent plus à améliorer le côté innovant de leur produit. La question est pourquoi ? Pourquoi avec de plus en plus de personnes impliquées dans un projet, plus de moyens financiers et d'autres avantages, les processus d'innovation semblent perdre de la vapeur ? Quels sont les solutions pour améliorer ces processus ? Et quels sont les difficultés rencontrées ?

Après une revue sur les besoins de la santé de demain et les innovations dans le secteur (dont nous avons brièvement parlé ci-dessus), nous exposeront une stratégie, qui existe parmi d'autres, développée pour améliorer la recherche innovante¹⁰. Enfin, un processus mis en place au sein d'une compagnie dermatologique pour trouver, analyser et suivre l'innovation sera exposé et discuté.

Mais avant toute chose, un bref résumé de la compagnie où s'est déroulé le stage s'avère nécessaire.

En 1981, Nestlé et L'Oréal ont créé une nouvelle compagnie pharmaceutique nommée Galderma. Le but de cette compagnie est de devenir leader mondiale en dermatologie. Le siège social est situé à Lausanne en Suisse. Mr Humberto C. Antunes est à la tête d'une compagnie de plus de 3000 collaborateurs et 5000 employés.

Galderma est centrée sur l'innovation à des fins médicales et esthétiques. Pour preuves, chaque année, 20% du revenu total est investi en R&D. Ainsi, la recherche et le développement au sein de la compagnie est à son pic de performance. De plus, il y a aussi une vocation internationale : Il existe 5 centres localisés à Sophia Antipolis (France), Princeton (Etat unis d'Amérique), Uppsala (Suède), Egerkingen (Suisse) et Tokyo (Japon). Les trois centres de productions sont localisés en France, au Canada et au Brésil. De plus, la compagnie est présente à travers le monde entier, des affiliations sont trouvées dans 33 pays. Les produits sont vendus dans plus de 70 pays. Chaque année, le chiffre d'affaire dépasse le milliard d'euros.

Comme Galderma investie en R&D, il peut offrir une large gamme de solutions médicales comme Différine®. Ce produit a été lancé en 1995 avec pour indication le traitement de l'acné modérée. Ce produit ainsi que Oracea® font partie du top 10 des ventes en dermatologies à travers le monde. Le portefeuille de Galderma grandit continuellement. A propos des aires thérapeutiques, Galderma est

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centré sur la rosacé, le psoriasis, l'onychomycose, les problèmes de pigmentation, les cancers cutanés (or mélanome) et même plus le vieillissement de la peau. Depuis quelques années, de nouveaux produits sont également disponibles en parapharmacies sous la marque Cetaphill®.

Un dernier point, Galderma est maintenant entièrement à Nestlé, qui a racheté la part de L'Oréal cette année (2015). Galderma est maintenant la partie prescription de Nestlé Skin Care. Un grand nombre de réorganisations sont en cours. Nestlé Skin Care a pour vocation de devenir le leader en innovation dermatologique. Ainsi de nouveaux centres ouvrent à travers le monde. Pour être plus précis, ce sont 12 centres d'Innovation Ouverte, appelés SHIELD (Skin Health Investigation Education and Longevity Development). Ces centres appliquent une nouvelle stratégie de recherche et développement tel que l'Innovation Ouverte ou l'Approvisionnement de foule (Open Innovation et Crowdsourcing). Ces stratégies ont été essayées pendant le stage.

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Where, who and how? Three questions about innovation

Current situation and future needs in healthcare

First of all, in recent decades, the world has witnessed major gains in life expectancy. A baby girl born in 2012 can expect to live an average of 72.7 years, and a baby boy up to 68.1 years. This is 6 years longer than the average global life expectancy for a child born in the early 90's¹².

This progression is more significant in low-income countries with an increase of 9 years between 1990 and 2012. This was possible despite the HIV's pandemic infection. The rate of children mortality is lower as well as the reduction in deaths from infectious diseases in adults. The country that has increased its life expectancy the most during the last two decades is Liberia by a rise of 19.7 years.

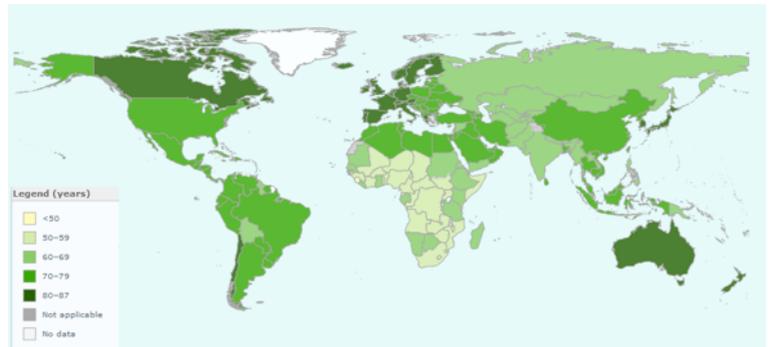


Figure 1 Life expectancy - WHO report 2012 – Source: a

As we get an idea of the life expectancy worldwide (Figure 1), we can think that it will not increase endlessly. Indeed the maximum life expectancy might be up to 150 years¹³. As a matter of fact, the whole population is getting older and keeping them in a good health is one of the biggest challenges especially with the chronic diseases.

Another fact to keep in mind is that life expectancy is different from one country to the other. The place of birth is a major consequence; it determines what are likely to die from. That brings us to the second point, which is the evolution of illnesses.

In the 1900's the main causes of death were due to infectious diseases such as tuberculosis. Nowadays, with the aging of population and more accurate therapies for infections, the leading causes of years of potential life lost are moving from infectious to chronic sicknesses such as heart diseases, diabetes and so on¹². As we see on the graph below (Figure 2) a lot of infectious diseases still exist. Furthermore they become chronic. For example, HIV has typically shifted from infectious to chronic disease. Indeed this pathology that used to kill a person within a few years can now be treated and almost controlled during decades. Thanks to the use of a three therapy

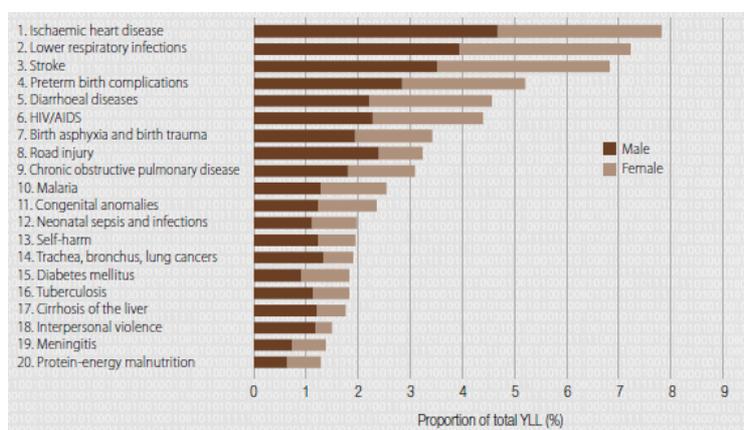


Figure 2 The 20 leading causes of YLL - globally, 2012 - WHO report – Source: a

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three times a day.

There is still a difference between high and low-income countries in the type of diseases responsible for premature deaths (Figure 3).

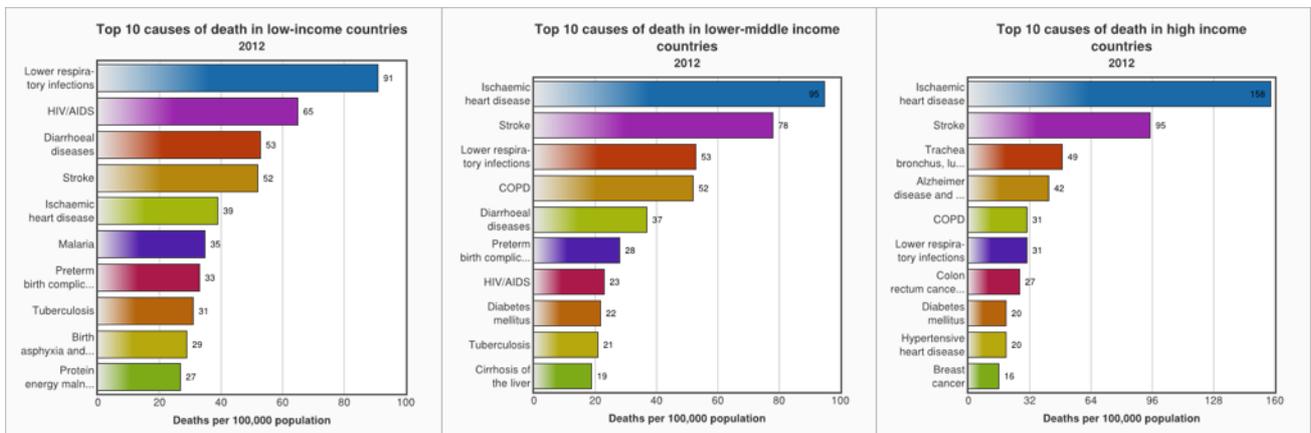


Figure 3 Top 10 causes of death in different type of countries - WHO report 2012 – Source: a

Observation can be made with these graphics; a large proportion of deaths lead by infectious diseases is attributable to developing countries while a large proportion of deaths linked to chronic diseases is attributable to westernized countries.

Through of explanation;

- Ischemic heart diseases is the main cause in high income countries while it stands only at 6th position in low-income countries
- On the contrary HIV is second in developing countries and not even at the top ten in high income countries, thanks to prevention, diagnosis and treatments available in Europe and so on.
- Mental diseases such as Alzheimer disease are more present in countries where life expectancy is higher. But like all western diseases it will be present worldwide as soon as the difference between countries will be reduced. The thing is we have no plethora of treatments for those kinds of diseases. It means that a huge effort is needed in this sector. Fortunately, answers do not always come from chemical or biological entities; health management for those sicknesses will be improved with IoT, connected devices and telemedicine.

As a society develops from a low to a high-income country, diseases also change. This is due to the change of way of life, access to healthcare, etc. Besides this, we can notice that some diseases existing only in the southern hemisphere are expected to move to the north because of the global warming, this must not be forgotten in the coming years... As an example, tiger mosquito, which carries malaria's pathogen agent and was eradicated from Europe over 60 years ago is about to be reintroduced because of the climate change¹⁴.

Management of those diseases while trying to be cost-effective for the society, and with the best quality of life for patients is also one of the main challenges of tomorrow's healthcare. It is crucial to define our future pathologies and adapt our system as well.

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We see that the aging of the population and the change in diseases will alter the needs of healthcare but not only.

Let's take the case of France's healthcare system; indicators of health are not so favorable, even though healthcare costs are among the most important in the world. That is why important progresses have to be carried out to improve public health while mastering the expenses¹⁵. The cost of health is one of the big challenges. Healthcare used to be curative (and is still curative for the most part). However it is evolving into a more preventive medicine (with probiotics, self-monitoring, diseases screening). Therefore, the cost could be drastically decreased. A better organization with exchanges between the healthcare professionals at the hospital in town and the use of a common patient file could improve public health. Lots of solutions are being discussed worldwide. China has proposed an affordable healthcare system compounded of a four-layer system: (1) wearable intelligent sensors and devices for p-Healthcare system (PHS). (2) Home healthcare system (HHS). (3) Community healthcare system (CHS). (4) Hospital health information system (H2IS). This four-layer structure should ensure that people are monitored by the new system as closely as it can. It results in the novel transformation of the function of the healthcare systems from symptoms treatment to early risk detection and prevention¹⁶.

While we think of the subject, several solutions can be proposed like the patient education, which shows huge benefits in chronic diseases¹⁷ but we would move quite far from the issue of this paper. That is why we are now going to focus on the innovations under development or already on the market for healthcare.

Overview of healthcare innovations, where are they at?

Since science exists, innovations exist as well. But some have really changed healthcare. For example, the discovery of Penicillin brought a major progress to the fight and the treatment of infectious diseases. Furthermore, vaccines started a new strategy against illnesses, which is preventive medicine rather than curative medicine.

Currently, our medicine is based on curative more than preventive. Most parts of the molecule used are chemical. The patient's compliance and monitoring are big challenges that have not yet been achieved. Vaccines don't give the best type of immune response and have had some controverted side effect.

As we will see further down, new therapies based on biological structures are taking market shares from chemical molecules. Lots of solutions are experienced for a better health management of the patient through wearable sensors, new medical devices or smart packaging. Personalized medicine is expanding in importance every day with theragnostic, nanotechnologies and diagnosis devices.

New vaccine strategies are on their way to be marketed with a new approach that triggers better immune responses with fewer side effects. In the same order, medicine is becoming more preventive through alternative treatments such as probiotics but also self-monitoring.

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All of these innovations, which are not exhaustive, merit to be more detailed. We will aim to understand what those health innovations are. After that we will go to the heart of the subject, which is the research for innovation applied to a dermatological scope.

Biological products

First of all, one big innovation in healthcare is the changing approach in therapy. Standard drugs used to be chemical, small and easily characterized. Innovative drugs are now biological molecules, which are bigger, more heterogeneous and hard to characterize. A brief comparison can be proposed:

Table 1 Comparison between small and biological drugs - Source: <http://www.gabionline.net/>

	Small molecule drugs	Biological drugs
Size	<1 kDa, single molecule	>5kDa, mixture of related molecules
Structure	Simple, well defined, independent of manufacturing process	Heterogeneous, defined by the exact manufacturing process
Modification	Well defined	Many options
Characterization	Easy to characterize completely	The molecular composition and heterogeneity cannot be characterized completely
Manufacturing	<ul style="list-style-type: none"> - Produced by chemical synthesis - Predictable chemical process - Identical copy can be made 	<ul style="list-style-type: none"> - Produced in living cell culture - Difficult to control from starting material to final API - Impossible to ensure identical copy
Stability	Stable	Unstable, sensitive to external conditions
Immunogenicity	Mostly non –immunogenic	Immunogenic

Observation can be made from this table; biological drugs are large and formed out of a heterogeneous mixture. They are made from engineered cells which can make various post-translation modifications such as glycosylation according to their own variability. Manufacturing is also a big challenge because any change, even minor, in the process can impact the final product's quality such as efficiency or immunogenicity. Moreover, all these problems have to be considered even when a company develops biosimilars¹⁸. The cost for a biological product (original or biosimilar) is much more important than for chemical drugs. This is due to the manufacturing cost, R&D process, stability's issue and so on.

Even with all these challenges, biological drugs offer new perspectives for the treatment of a large amount of diseases currently with no available treatment or a poor therapeutic arsenal. It also tends to make tomorrow's medicine more personalized and accurate.

A classification of biological product, which includes biotech and advanced therapy, proposed by Leem Biotech and Genopole, is presented below:

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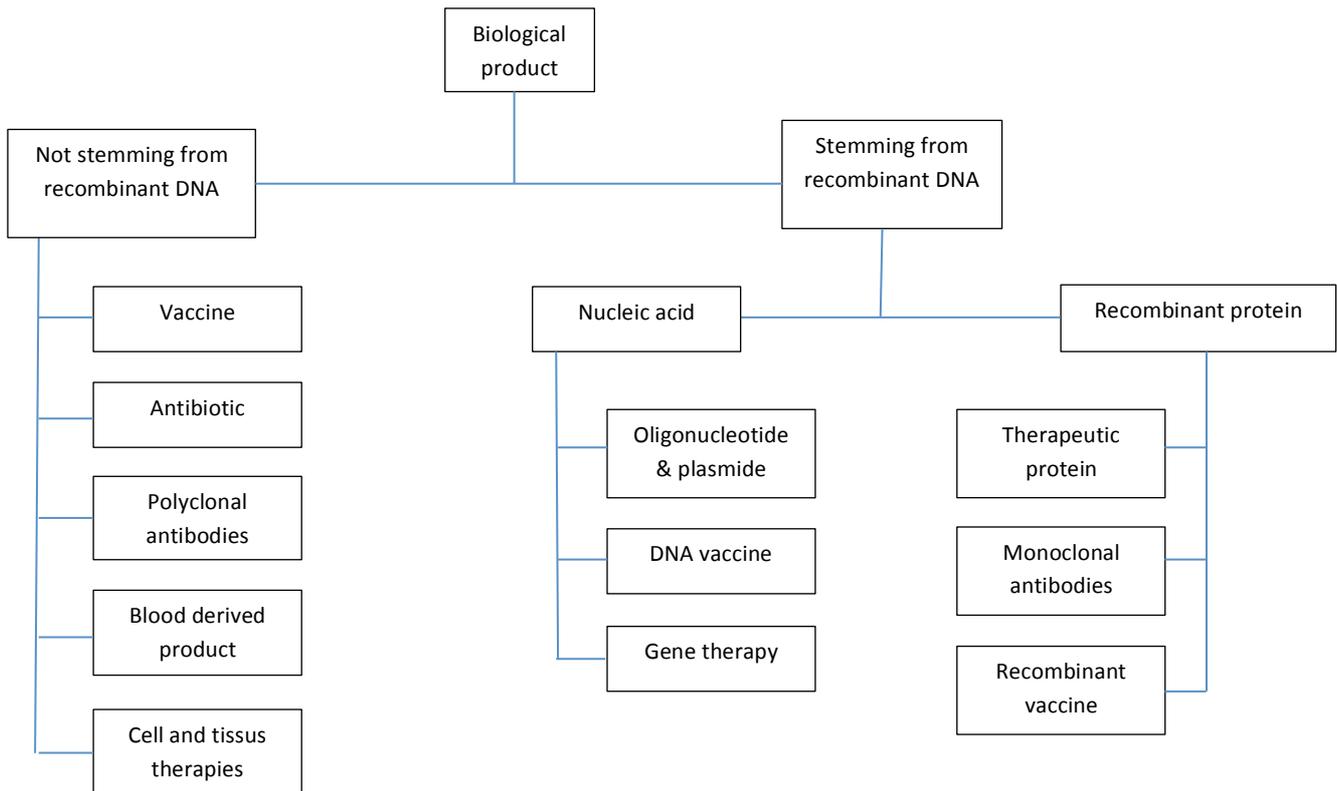


Figure 4 Classification of biological product - Source: Leem & Genopole, Développement & conseil, 2008

Using this chart above, we can make several remarks:

- Biological products stemming from recombinant DNA are linked to biotechnologies
- Are considered as advanced therapy medicinal products (ATMP) such as gene therapy medicinal products, somatic cell therapy medicinal products and tissue-engineered product¹⁹.
- Vaccines are classified in different categories depending on their characteristics and method of productions, and we will explore that later.
- On the one hand, polyclonal antibodies are extracted from immunized or healthy donor. On the other hand, monoclonal antibodies are made by hybridomas or with a transfected host-cell in fermenter. Antibodies are really full of interest because they have several fields of application, from autoimmune diseases to cancer including diagnosis and many more.

Now we are going to give more details concerning biotech, ATMP and vaccines.

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Biotechnology

Every biological product stemming from recombinant DNA can be considered as biotechnology's product. Since the early 20's and the extraction of the insulin²⁰, biological products began to be used for medicinal purpose. At that time, the products of biological origin were extracted from animals or plants. Nowadays, we

Definition of biotechnology proposed by OECD: *"The application of science and technology to living organisms, as well as parts, products and models thereof, to alter living or non-living materials for the production of knowledge, goods and services."*

produce them by using biotechnology, which has been used since antiquity to transform food or beverages. Making wine is a biotechnological process performed by yeast. But the difference is that we can now act on the genome of the cell with the aim of making them produce a substance that they aren't able to do naturally, such as insulin. Biotechnology is the premier global economic growth opportunity of this new century. It is formed out of 3 sectors which are: Red biotech for medicinal and pharmaceutical products, green biotech for developing agricultural and environmental tools and white biotech for industrial scale use²¹. Here, we are going to focus only on the red biotech.

Products stemming from recombinant DNA are shared by two categories: Nucleic acid and recombinant protein.

Concerning nucleic acid therapeutics, they are based on nucleic acids including antisense oligonucleotides, aptamers and small interfering RNAs. Their function consists of the specific inhibition of the function of a particular gene involved in the disease. DNA vaccines are made of DNA vectored in host/patient's cell. Then the DNA will be transcribed into a protein that will activate the immune system triggering a protection against the disease. This will be discussed in the chapter dedicated to the new vaccinal strategies. The resulting protection is better than the one given by classic vaccines used with adjuvant. Gene therapy will be handled with ATMPs. Compared to recombinant protein, nucleic acid therapeutics' application are still really limited with only a few products on the market but it is a very promising arm of the biotechnologies.

Recombinant proteins are produced by cells into a fermenter. Those cells can be bacteria, yeast, insect or mammalian. Beforehand, they have been genetically modified by, for example, integration of a plasmid by multiple methods: Infection by genetically modified virus, transfection by plasmid contained in nanoparticles or still physical integration (with ultrasound).

To get a better idea of the complexity of production of recombinant protein, we can have a look at figure 5, which represents a basic workflow, among others, for production of a recombinant protein; every step has to be monitored because, as we saw previously, any change in the process can change the final product. Up-stream process includes cell's transformation, cell's culture and protein extraction. Indeed, once the culture has grown enough the protein has to be extracted. A basic method is sonication which consists of the destruction of the cell with ultrasound. Then the protein has to be purified, this is the purpose of the down-stream process.

The complexity of down-stream process is not the purpose of this paper but we can notice that it is a crucial step that has to be well controlled to avoid any loss of yield.

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All these steps are designed in the laboratory then the scale up is performed to expand the process at an industrial scale.

Quality controls are performed throughout the process to ensure that the product will respond to the criteria needed for therapeutic use. Batches, among them, have to react exactly the same way as those controlled.

Recombinant protein subdivides in three categories:

- Therapeutic proteins that include growth factors, hormones, cytokines, proteins of fusion, plasmatic factors and enzymes.
- Monoclonal antibodies (mAb), which support a huge increase by taking most part of the market

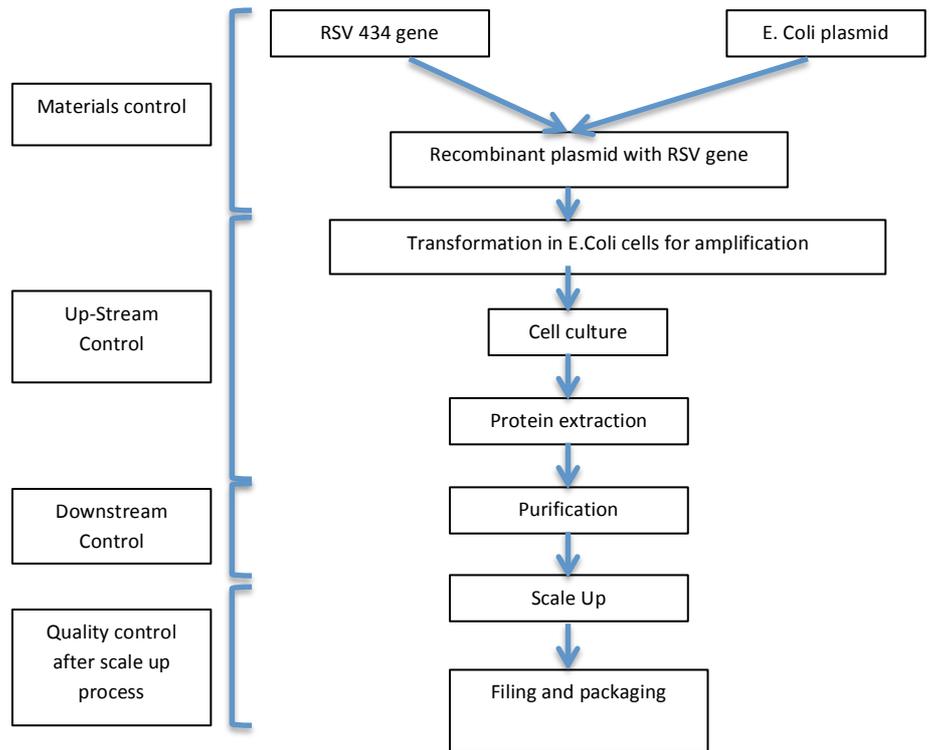


Figure 5 Workflow of the production of a nanobody during "The drug project" within Grenoble University of Pharmacy in 2014

year after year. First imagine in the 70's this type of protein used to be made by hybridomas formed out of an immune murine cell that produced an antibody against a specific target and an immortal cell. Since that time, mAb used to be murine but there were problem of immunogenicity after the injection to humans. To avoid that, genetic engineering transformed mAbs to make them more "human".

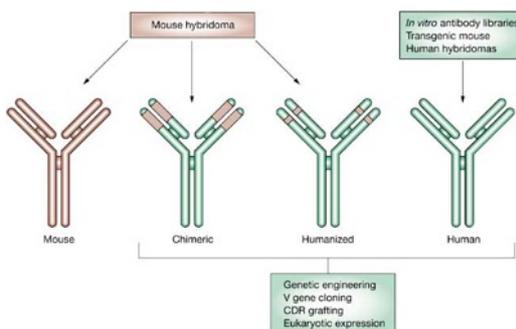


Figure 6 Different type of mAb, as it becomes human the murine part (in red) decreases - Source: b

A second type of mAb was thus created: Chimeric. Then, with an increased percent of human origin a third and a fourth generation were created, respectively humanized and human. An overview of those different categories is given on figure 6. Therapeutic areas targeted by mAb, which are outstandingly varied, are diseases with a big unsatisfied need. The main players are Genentech / Roche, Abbott, J&J, Biogen Idec, Amgen, Novartis²² but lots of start-ups, focusing on biotechnology contribute to mAb's development.

Labiotechmap.com provides an overview of the companies within the European Union. Therefore we can see that there are more than a thousand companies only in Europe and many more around the globe.

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Something that seems important to notice is that mAbs are evolving. Indeed a new generation of products appears to be more efficient, accurate, etc. These products are bispecific antibodies, which consist of two different monoclonal antibodies, which are capable of simultaneously binding to two different targets. However these products are at a preclinical or clinical stage and only two of them are marketed. According to this, we can say that these innovative products are in constant change. To put it in simple term, let's say that "classical" mAbs and bispecific antibodies are a part of a family named monoclonal antibody.

- Recombinant vaccines have two subtypes: Subunit vaccines such as B hepatitis vaccines and vector's vaccines which is a genetically modified virus (example Cholera vaccine) but vaccines will be explained in detail later.

As we saw, biotechnology is made of several types of biological products. They are not all cited above because other products are still at an early development stage (e.g., bispecific antibody) and we would like to provide an overview of what is available instead of an exhaustive list. These products show a great number of applications and promises for healthcare. However, we must keep in mind that all the production processes have to be known and mastered, which is more complicated than with chemical processes.

Furthermore, as this technology can serve the good common it can also help some criminal organizations. For instance, recent discovering has isolated gene responsible of the synthesis of opioids in plant. Those genes can be implemented in yeast and lead to a production "hand-made" of drugs... This has been highlighted since the first DNA recombination in the 70's but must be kept in mind.

This is only a part of the innovations currently available in healthcare. Let's continue our exploration of this subject by going through ATMPs

Advanced therapy medicinal products

Concurrently, advanced therapy medicinal products (ATMPs), which include gene therapy medicinal products, somatic cell therapy medicinal products and tissue-engineered products¹⁹, is developing as well.

A regulatory aspect is crucial to understand what ATMPs are. In Europe, two regulatory aspects are distinct and complementary; on the one hand, tissues and cells from human origin (Directive 2004/23) and on the other hand, the ATMP (Regulation 1394/2007)²³.

Concerning the directive 2004/23, it shall apply to the donation, procurement testing, processing, preservation storage and distribution of human tissues and cells intended for human applications. It also applies to manufactured products derived from human tissues and cells intended for human applications.

This directive does not apply to tissues and cells used as an autologous graft within the same surgical procedure, blood and blood components as defined by Directive 2002/98/EC and organ transplant.

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On the contrary, Regulation 1394/2007 defines ATMPs, which are gene therapy, cell therapy and tissue engineered product. So we can conclude that ATMPs are engineered cells or tissues while directive 2004/23 describes tissues and cell not engineered that are used as it stands.

The purpose of the gene therapy is to provide a missing gene to the patient's cells. Because of this missing gene the patient has a disease. As we provide the gene, we can hope a recovery of the patient. To vectorize the gene to the patient several strategies are available: Virus like Adenovirus or Herpes Virus can be used as well as nanoparticles like linear polyethylemine derivative.

The big success, with grey areas, of gene therapy reminds us of the gene transfer strategy in X-SCID patients²⁴. Those patients suffered from X linked severe combined immune deficiency (X-SCID). The strategy was to inject the missing gene to restore immunity. The problem was that in 3 patients, an insertional mutagenesis occurred, leading to the death of 1 patient. This was due to the vector that inserted the gene in an unwanted place in the genome leading to the activation of an oncogene. Several strategies, like suicide gene, have since been then developed²⁵ to avoid this.

So, as we see, gene therapy can restore physiological functions that are not present in some diseases but we have to be very careful because an adverse event can occur rapidly. Moreover there are lots of ethical barriers; for example, gene therapy is forbidden for germ cell. Indeed, we are not allowed to change something that will be transferred to the offspring.

Now, regarding cell therapy (CT), we can firstly ask ourselves three questions:

- What type of cell for CT?
- What is nowadays' CT?
- What is tomorrow's CT?

First of all, the type of cell used for CT is stem cell. This type of cell has three characteristics which are: auto renewal, differentiation of a single cell toward several lineages and the capacity in vivo of one cell to reconstitute at least a tissue in the long run. The origin of those cell can be blood or mesenchymatous or even embryonic and so on. Some cells such as fibroblast can be induced to become pluripotent; they are called induced pluripotent stem cell (iPS)²⁶.

The second question is: what type of therapy exists today? Two indications have been validated: Graft of hematopoietic cell and autogenous transplant of keratinocytes for severe burns. In a near future, lots of applications can be expected such a cardiac cells graft after a stroke. This strategy is developed at the hospital Saint Louis in Paris. The last trial on the subject provides very encouraging and promising results²⁷.

Last point concerning ATMPs is about tissue-engineered products. This kind of product, defined by regulation 1394/2007, contains or consists of engineered cells or tissues. It is presented as having properties for, or is used in or administered to human beings with a view to regenerating, repairing or replacing a human tissue. It may contain cells or tissues of human or animal origin or both. But one thing to be underlined is that it may also contain additional substances such as cellular products, bio-molecules, bio-materials, chemical scaffold or matrices. As an example of this strategy, we can mention Chondroelect[®], which is a graft of an autologous chondrocyte already available on the market²⁸. Although the Committee of HAS (Haute Autorité de Santé – French regulatory agency)

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believes that it is an innovative biotechnology, the actual benefit of Chondrocelect® must provisionally be regarded as insufficient to justify its reimbursement, given the current state of the data. That means that once again it is not because it is innovative that it brings more than current therapy.

After this non-exhaustive summary about innovative therapies, our focus will be directed to vaccination, as it is a pillar of the preventive medicine. A great many strategies are already available or being researched.

Vaccination

The way that we provide healthcare changes since the discovery of rabies vaccine by Louis Pasteur. Indeed, high-income countries have no more worries with infectious diseases in part through the vaccine; unfortunately, it is not so for under developed ones. We noticed that cause of death in poor countries remains mainly infectious¹². From the early beginning, three generations of vaccine have been developed and are summarized in the table below:

	Development	Type	Manufacturing	Example
Traditional vaccine	First generation	Inactivated	Made from whole virus or bacteria	Vaccines for Cholera and A hepatitis
		Attenuated	Made from the part of the organism responsible of the illness	Vaccines for rubella, yellow fever
		Toxoid	Inactivated toxin which immunize against specific bacteria	Vaccines for tetanus and diphtheria
	Second generation	Conjugate	Contain protein of the external cover of the organism responsible of the disease	Vaccine for the flu <i>hemophylus influenzae</i>
		Subunit	Contain one or several components of an organism which are responsible for the disease, rather than the whole organism, to stimulate immunity	Vaccines for B hepatitis and malaria
		Deletion of genetic material	Genetic deletions guided by the identification of genes responsible for the virulence, for the colonization, for the capacity to survive in cells	Vaccines for Herpes and Cholera
Recombinant vaccine	Third generation	Recombinant	Produce by using technology of recombinant DNA, there are two type of this vaccine: Subunit and vector	Gardazil which is for papillomavirus
		Therapeutic	Develop to treat diseases mainly cancer	Under development
		DNA vaccine	DNA which is translated in the host cell one or several protein of an organism responsible for disease. Produced proteins act like an antigen that stimulates immunity	Under development

Figure 7 Description of the different types of vaccine - Nature, Développement & conseil 2008

Compared to other treatments, vaccine is administrated only once (most part of the time) contrary to long-term treatments required for chronic diseases. As a consequence of this, commercialization of Gardasil in 2006 in USA generated a revenue of 175M\$ in 6 month but in 2007, sales went from 312M\$ for the first quarter of the year to 286M\$ for the second quarter²². These new vaccine strategies sound better for preventive medicine rather than for pharmaceutical companies' business. Besides this, the market of recombinants vaccine is at an increasing stage with few products on the

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market and many more on research. They are in competition with traditional vaccines which are at a more mature stage. The big drawback of recombinant vaccine remains the development cost²².

Third generation vaccine has a big advantage compared to second one vaccine in the way that second generation vaccine needs adjuvants to increase the immune response. Those adjuvants, especially aluminum, are controversial. So how can we have a bigger immune response without adjuvant.

To grasp the topic, before answering the previous question, we need to know a little more about immunology; an antigen can give two types of response: Humoral response (Which is antibody mediated response) and cytotoxic T cell response (Also known as cellular response).

Second generation vaccine (which contains aluminum as adjuvant) gives a higher humoral response but on the other hand a weak cellular response. Immunity is also systemic rather than local (also called "mucosal immunity"). Local immunity provides a good defense because pathogen agent goes through mucosa to get into the body. Because of this immunity, pathogens can be stopped before entering the body.

Ideal vaccine has to be immunogenic, with a complete immune response (humoral and cellular) but with a systemic and a local response too. On one hand, protection has to be long, and on the other hand security has to be optimal. Indeed because vaccines are preventive therapy, people do not accept any adverse effect... Even if every medication is a poison and zero risk does not exist.

To give a good response, antigen's conformation is really important as well as the distance between two antigen, even the particular form. That is why third generation vaccine tries to mimic more the natural pattern of immunity. The strategy consists in adding antigen to a vector. In this way, antigen is better presented to the immune system and do not require adjuvant to increase the response. Another strategy, as we saw previously, is DNA vaccine which will bring into a cell a DNA fragments that will be translated into protein inside the cell. Those proteins will be presented from the inside of the cell and not from the outside like with subunit vaccine (which contains proteins as well but they never find themselves into the intracellular environment). And because of this intracellular presentation, immune response will be improved, thanks to DNA vaccine.

Regarding therapeutic vaccine, most part is developed to treat cancer but there are other indications (e.g., inflammatory diseases as well as autoimmune ones). Since early 1900's we know that some viral infections help sick people to recover from a cancer. Indeed, if a virus goes into a cell, immune system trends to suppress this infected cell. If this cell is a cancerous cell it is a winning situation. We also know that there is a cancer immunosurveillance process that protects immunocompetent hosts against primary cancer development²⁹. A cancer in which T-cell infiltration is associated has a favorable prognosis³⁰ too. While acknowledging all this, it is easy to imagine a therapeutic vaccine: It's a vaccine which contains proteins found in a cancerous cell able to activate immune system that will defend against primary cancer development. Or a vaccine formed out of virus which will recognize tumor and then, once inside damaged cell, will trigger immune system as well. These are the two main approaches for therapeutic vaccine against tumor.

After this overview about innovative therapies, we are going to deal with other types of innovation, which do not concern molecules, but devices, technology and services that can improve healthcare.

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Medical and wearable device

Since few decades, technology has drastically improved its performance while it has been miniaturized. Improved batteries permit a bigger range of action too but it remains the main problem of devices, which require electricity. Besides this problem, many things can be considered as a medical device, for example:

- Medical device can be a help for administration;
- It can be a diagnosis tool;
- It can be an implantable device such as pacemaker, a prosthesis or even a stent;
- It can be a device for monitoring a biological parameter (Blood pressure, heart beat and so on);
- But it can also be an application or a software dedicated to healthcare or health management

So medical device is very wide terms that can be applied to a bandage as to a device of magnetic resonance imaging. Furthermore lots of medical devices (MD) are a combination of a medicine and a device: For example, a syringe pre filled with a drug is a medicine product, on the contrary, an empty syringe is considered as a MD³¹.

Nowadays, MD can predict, prevent, diagnose and treat many diseases as well as to relieve functional problems via treatments and technologies which were not conceivable few years ago. While certain innovations come from the research, many are those who come from other industries and are adapted in biomedical field. Development of different industrial fields in health (such as biotechnology...) and of new technologies (nanotechnology...) gives the rise to innovations in the sector³¹. As we saw previously, aging of the population coupled with an increase of chronic diseases but not only (development of evidence-based medicine and of prevention and detection program for cancer, HIV and others) are further factors which may trigger innovation finding for MD. Medical device becomes smart (due to technology) connected to its environment, more biocompatible with a wide range of application. The MD business is increasing every year. It is also a cornerstone of theragnostic, which is going to be developed in few pages.

Wearable devices (WD) can be considered as different from medical device in a way that they have not always medical purposes. Furthermore WD is designed to gathering data to monitor your health. That enters in the definition of a medical device, which is wider (e.g., an MD can treat a disease). These data can be considered as health data or well-being data. As a manufacturer uses one definition rather than the other, regulatory aspect will be impacted. Indeed, well-being data are gathered to allow you to preserve your health capital. As a matter of fact, it can be considered as a well-being data your heart rate or the amount of step you make every day. Besides this, health data are critical, because they are gathered to control a pathological state (e.g., blood sugar and insulin for diabetes' management). Because of this, accuracy and efficiency of the device have to be perfect. To be sure that WD, which collects health data, will fit with expectation of health agencies; manufacturer develops them as a medical device.

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To sum up, on one hand wearable device made for gathering well-being data are considered as a “gadget” so there are not many regulatory issues, on the other hand, WD which collect health data are considered as medical device. These last devices need much more qualification before marketing.

As an example, let’s discuss about smartwatch that are developed by big companies like Apple or Samsung. At first sight, they have no medical purpose, they are more or less a remote for your smartphone, but these little things full of sensors can monitor your health. A good example is that lots of watches help you monitor your physical activities, your sleep and so on. By monitoring this, they monitor your health through well-being data. More interesting, tomorrow’s smartwatch might be able to analyze your blood and will detect early stage of a disease development. This will drastically improve health management, medicine will be more proactive, and that will reduce the cost. For the moment, accuracy of these objects is not acceptable for medicinal purpose. Indeed, from one smartwatch to another, heartbeat can vary up to 20 beats per minute. Furthermore, if they will monitor health data, rather than well-being data, they will need many more validation from health agencies. Therefore, all those aspects have to be considered since a smartwatch will gather health data but for now it is only well-being data.



Figure 8. Example of several smartwatches
– source: c



Figure 9. UV sensor –
source : d

Other type of wearable device like a UV-sensor connected to your smartphone will help you to manage your sunscreen application as well as track sun-generated vitamin D³². This is possible only because of a UV-sensor, which detects UV A and B and an algorithm to determine the dose received. Those kinds of sensor might be ubiquitous in a decade. Until now, they are not considered as medical device. But if we take the same device to monitor your UV exposition during a phototherapy, once more, accuracy has to be perfect so the validation will be harder to be obtained. Furthermore the label “Medical Device” will be needed.

At last, but not least, evolution of medical device allows also an improvement of quality of life. For example, someone who loses his leg in an accident for instance, will be able to walk or even run like any ordinary person; thanks to microprocessor and new materials used in his prosthesis. Furthermore, new medical device permits a better delivery of drugs or a better treatment of certain diseases compared to conventional one.

For the purpose of this paper, we focused on self-monitoring, but as referred above, medical device is a wide range of tools (e.g., diagnosis tool, prevention, treatment of a disease, a wound or a handicap, or the study or the replacement or the modification of the anatomy or of a physiological process).

To conclude on this short overview of medical and wearable device, innovation in the field comes from the connection of the device (e.g., Internet of Thing), the miniaturization, the technological improvement made during these last decades. Self-monitoring will allow early detection of diseases; therefore an improvement of preventive medicine and, in the end, the cost is diminished as well as better quality of life. The difference between a medical device and a wearable device (in the medical field) can remain unclear or confusing; the easiest way to differentiate a MD and a WD for self-monitoring is the type of data gathered.

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Nanotechnology

Nanoscience and nanotechnology involve the ability to see and to control individual atoms and molecules. It is really recently that we got the ability to see at nanoscale, about 30 years ago. Today's scientists and engineers are finding a wide variety of ways to deliberately make materials at the nanoscale to take advantage of their enhanced properties; such as higher strength, lighter weight, increased control of light spectrum, and greater chemical reactivity than their larger-scale counterparts³³.

Definition of nanotechnology proposed by

Nano.gov: "Nanoscience and nanotechnology are the study and application of extremely small things and can be used across all the other science fields, such as chemistry, biology, physics, materials science, and medicine."

In the light of this, we can imagine that a great number of applications can be proposed to medical field, which is true. Nanotechnology can be used as a vector to bring treatment directly to the target; two scientists have created a robot made of a complex 3D structure of DNA strands (*Figure 10*). It looks like a barrel that contains molecules. This barrel recognizes some combinations of cell-surface proteins and then it is opened to deliver the drug right to his specific target³⁴.

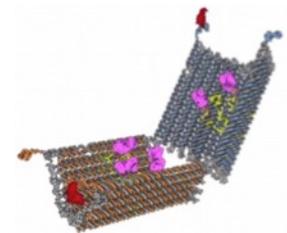


Figure 10. Nanorobot, barrel, source: e

Nanotechnology can be also useful for packaging; relevant example of this is the development of nanocoating that does not allow bacteria's growth on the treated surface³⁵. This may avoid the using of anti-microbial agents, which are controversial. Nanocoating can also be applied to MD to avoid development of biofilm.

Diagnosis is also improved by nanotechnology. As a matter of fact, a tool for single-virus particle detection is under research; it is likely to revolutionize diagnosis for life threatening virus infections³⁶. This kind of technology will be available as much for bedside diagnosis than during humanitarian mission. These new tools are called "lab-on-a-chip", which are micronized technology such as PCR or micro array. This has reduced the time of experiences, volumes of samples and raw materials.

Nanotech has also improved imaging diagnosis, by developing new methods and increasing the resolution and sensitivity of existing techniques. For example, new contrast agents, are formed by synthetic and biological nanoparticles that improve sensitivity and resolution³⁷.

Concerning tissues engineering, a part of advanced therapies, nanotechnology provides instruments that can accelerate progress in the engineering of organs. Because cell based therapies are nanosized, using nanotechnology can improve localizing, recruiting and labeling stem cells to begin the regeneration process³⁸ much more than the usual technologies.

As a conclusion, nanotechnology is a kind of support's technology because it can be applied to several fields such as vectorization, diagnosis and so on. Furthermore it will play a big role in tomorrow medicine as much as other field like environment (e.g., one day, scientist might develop Nano-Robots that will depollute water from hydrocarbon).

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Packaging

Because innovation is everywhere, it is ordinary to find some in packaging. Indeed, many things are under research. For instance, in a pharmaceutical company, packaging is something major. Because it interacts with the customer and at the same time it also protects the product. As a matter of fact, a packaging made for a cream nowadays has not a great number of functions. The one we can refer to: Protect, inform, to measure out the product (e.g., dosing cap).

In the light of this, how a packaging can be improved? Simply by increasing the relation with the customer or providing a better protection. Moreover something that has to be considerate is the environmental aspect. The matter used for manufacturing the product has to be eco-friendly. And last, but not the least, monitoring the product's intake can be a path of innovation.

Now that we brought out these four paths that can lead to innovation, we are going to identify several innovations for each one.

Regarding the relation with the customer, it can be improved in several ways. First, the patient wants to have information about the product, to know how to use it properly. Two simple ways to do that: Adding a quick response code also known as QR code. This is a flash code as you can see on the picture above. Scanning this code through your smartphone will redirect you toward an Internet page, where you can find information about the product or little video that explaining you the good use of the product.



Figure 11. Example of QR code – source : f

Another way to provide information is by adding a Radio Frequency Identification tag (RFID). Therefore you can scan this with a smartphone and then be redirected on a website. Either a RFID tag or a QR code connect your product to your smartphone, it is a part of the internet of thing. As we said, IoT trends to connect everything.

Something that companies neglect to mention is that every time a customer scans his product information is given to them. Therefore, they will know much more about you; where you use your product, where it has been sold and so on. It improves the Customer Relationship Management (CRM), which aims to provide better services to clients and gain their loyalty. We can say that is a win-win situation: Customer and company as well will be informed.

We can think that adding a tag to a packaging is not as innovative as that, but the thing is now the product is connected to internet, therefore much more information can be provided. It also makes the anti-counterfeit strategy better. QR code will be reviewed more in details in the results section.

As it will be exposed in the results, there are smart caps under development. These caps, connected to internet, can determine several parameters: When did you open the packaging for the first time, did you take your product or not. Therefore it can react consequently. Regarding creams, we know that most part of the time, after 18 months the cream expires (as an example) but we never keep in mind when we first open it. This question can be answered by the smart cap. Furthermore, if we miss an intake, the smart cap will be aware and then send you a text through your smartphone. It might improve drastically the compliance and avoid side effect.

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Regarding the protection of the product, as referred above, Nano-coating permits to avoid contamination of the product because of the surface bacteria cannot stick to the packaging, it remains clean. Furthermore, hydrophobic coating increases the restitution of the product because nothing remains in the bottle. Another innovative idea is to add some sensors in the packaging, thus we will know if a product is well preserved or not. As a matter of fact, if there is a thermometer in every packaging that needs to be kept in cold places, there will not be any doubts on the integrity of the cold chain.

The last approached point concerns the matter used in the product. As we all know, plastic is a poison. It is very polluting. There is actually a continent of plastic floating in the middle of Pacific Ocean even though the first plastic bottle was marketed in the early 60's. It is not possible, with the consumption society, to continue making packaging with this kind of matter that will end up in the sea. Furthermore, incinerating is not a solution too. That is why it is crucial to produce a sustainable packaging. This might be the most important innovation of pack regarding the Earth. Some alternative to plastic already exists like the use of biodegradable films for food application form out of gelatin³⁹. It is really important to focus on sustainable matter for production; the Earth is dying because of our carelessness. A quick reaction is urgent and necessary; the customer is really concerned of this. Providing him with these alternatives packaging could have an important influence on him, then he will prefer our product. Again, it is important to find a win-win solution.

Here are some innovations existing in packaging. To be innovative, the primary thing to do is to determine either problems and needs that a packaging can answer. Once attributes are listed, solution for each point can be found. The big trend is that companies are now providing a service rather than a product. Most part of innovation starts from this.

Alternative medicine; Case of probiotic / Cosmeceutical / Nutraceutical

Focused on dermatology, three alternatives show interest for investigation; probiotic, cosmeceutical and nutraceutical. These words might sound stranger to a lot of people. Nevertheless, they will be ubiquitous in a decade. Alternative medicine can be considered as innovation in health even if some products are used since Stone Age. Indeed, they can have now their own place in health management because they may, among other properties, prevent diseases or reduce symptom. Alternative medicine might be integrated in the preventive medicine of tomorrow, so a summary on the topic does matter for the purpose of this paper.

Everyone already knows probiotic, which can be defined as living microorganisms, preferably of human origin, that upon ingestion in specific and sufficient numbers confer unspecified health benefits to the host⁴¹.

Besides this, a cosmeceutical is a cosmetic product; therefore it is only topically applied. Moreover, it has biologically active ingredients, which provide medical or drug-like benefit.

Nutraceutical, also known as functional food, is an ingredient that provides health benefit for consumers. It can be complementary nutrients added, such as vitamin D to milk or it can be an ingredient used in cooking such as Konjac. A part of nutraceutical is nutricosmetic which provide health benefit to skin. A simple example is the vitamin C, which provides a protection against the impact of free radicals in skin.

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All these terms are new and sound like alternative to conventional treatment. Alternative medicine is something really trendy because people do not like chemical drugs; they trust nature to reduce any risk. At least it is what people think. After a presentation of several examples, two questions have to be answered: Does it really bring benefit for health? Is it really risk-free?

Regarding probiotic, it is a relevant strategy for skin health, because skin has a complex microbiome. This wide population of bacteria, fungus and virus play a significant role often unappreciated in human health; by providing direct benefit or simply prevent fellow harmful microbes from establishing residence⁴². On the other hand, dermatologists hypothesized that emotional stress could alter normal intestinal microbiota, increase intestinal permeability and contribute to systemic inflammation. In recent years, aspects of this gut-brain-skin theory have been further validated via modern, scientific investigations⁴³. In the light of this, we can imagine that probiotic may represent interest for skin condition. One example is *Lactobacillus acidophilus* that already is widely used as a probiotic. This bacterium might bring benefit for gut health, therefore a healthier organism and consequently a healthier skin.

It is sure that probiotic acts on health but are they really needed or a good diet can be enough? Further investigations are needed but will come up in the coming year even if there are already a great number of publications on the topic. In any case, probiotic has favorable opinion regarding to population. That is why many companies try to develop it.

Concerning cosmeceutical, first interesting comment is that FDA does not recognize any such category as “cosmeceuticals”. A product can be a drug, a cosmetic or a combination of both, but the term has no meaning under the US law. Moreover, on the EMA’s website, there is nothing that matches with this term. A simple example of cosmeceutical is moisturizers with sunscreens; it has both a cosmetic action (moisturizer) and a drug action (sunscreen). It is not a new term; it was first exposed more than 30 years ago by dermatologist Albert Kligman, but remains often controversial⁴⁴. Anyway dermatological companies start speaking about this and might use it as a claim for brand



Figure 12. Konjac powder
– source : g

new product. This might please the consumer and here is the final reason.

For the nutraceutical or functional food, we can expose the case of Konjac, which has no dermatological purpose but that is widely used and very trendy for westernized countries. Moreover, this example is relevant for the adverse event that can appear with such kind of product. Konjac has long been used in China, Japan and South East Asia as a food source and as a traditional medicine.

A gel prepared from the flour has been used for detoxification, tumor-suppression, blood stasis, alleviation and phlegm liquefaction⁴⁵. Furthermore, in westernized countries, Konjac is used as an appetite reducer because of the flour, which multiplies his size in the gut. Therefore, we can say that this food has pharmaceutical properties. As we all know: Because a poison can be a drug, a drug can be a poison. Konjac is not an exception to the rule: Using the Konjac as appetite reducer can bring shortages. Besides this, cases of hypersensitivity have been reported.

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Another example of adverse event regarding to functional food is the use of stimulant made from the plant (e.g., guarana, ephédra, colanoot) as an appetite suppressant. They can bring a great number of adverse events linked to amphetamine (e.g., insomnia, weakness, cardiac disorders).

As a conclusion, we can say that there are many alternatives to conventional treatments. These come with new designation and claims. They might bring new approaches, which show interest for health management. But we cannot forget that they might have adverse effect like any drug too. Furthermore, all those alternative medicines are not going to help in any case if we kept our everyday way of diet. All alternatives are not the main solution to our health problems, changing our way of life will bring us naturally alternative solutions because a good food has pharmaceutical benefit as well as exercising 30 minutes per day. Nevertheless, these are innovation and will be a part of tomorrow's medicine. Even if they exist already, they will be more ubiquitous tomorrow.

Now that some innovations regarding technology have been presented, we are going to expose a new way to treat disease. As discussed above, some drugs do not suitable for the patient, therefore adverse events may appear. To ensure the efficiency of a treatment, meaning that a patient will be a good responder, theragnostic has been designed. Let's explore this strategy in more details.

Theragnostic

First of all, with theragnostic there are three possible scenari⁴⁰:

- Therapeutic product followed by diagnostic
- Diagnostic product followed by therapeutics
- Co-development (e.g., Herceptin and HerceptTest for breast cancer)

Regarding the co-development, nanotechnology can permit combinations with single particles, therefore diagnostic and administrations of the drug are done at the same time.

The purpose of theragnostic is to provide a personalized medicine for every patient and disease. As defined in the introduction, theragnostic is developed around four bullet points:

- Biomarker of a disease
- Device for diagnosis the presence or the absence of this marker
- A therapeutic for responding patient
- Device for monitoring biological parameters during the treatment, therefore we can react before an adverse event comes out

Theragnostic is held by bioinformatics, genomics, proteomics as well as metabolomics. These tools generate the genetic and protein information required for the development of diagnostic assays⁸. Because of theragnostic, we act at every step of the treatment. At the beginning, it allows to develop efficient new targeted therapies with adequate benefit/risk to patients and a better molecular understanding of how to optimize drug selection⁸. During the treatment, theragnostic aims to monitor the response to the treatment, to increase drug efficacy and safety. Therefore this strategy might avoid unnecessary treatment. And then, after the treatment, to continue to monitor the patient's biological parameters allows to detect an early relapse.

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This approach is really innovative and shows a lot of promises, especially for cancer. Indeed, cancer therapies are very toxic for the body; use chemotherapy is not the best solution. There are too much adverse events (AE); sometimes people get sicker than if they take nothing. On the other hand, it is true that if they are not treated they might pass away but with conventional therapy they are not even sure to have a longer life time. Thanks to theragnostic we can imagine than treatment will be more efficient and because there is a selection of responder before the administration as well as an enhanced monitoring. Study showed the benefits of such approach in cancer in well-defined sub-populations of patients⁸.

Something important to notice is that new therapies are expensive. Because of financial issues, authority that pays for treatment, like France, needs to be sure of the efficacy of the strategy. Furthermore it can avoid over cost due to AE. So theragnostic has also the ability to reduce the expenses of a healthcare system.

To conclude on the subject, theragnostic is the big trend of tomorrow's medicine. Moreover, it may change the usual business model of pharmaceutical companies from the classic blockbuster model toward targeted therapies⁸.

As we saw, there are many innovations met in healthcare in every field. Moreover they might be other hidden today but will appear obvious in few years. Those entire innovations show interest for pharmaceutical companies, either big medium and small ones. Many want to have their proprietary biological drugs as well as their functional food and everything presented in between. But, nowadays who are the most innovative companies? Is it start up or big company? And how can a company be innovative with the current tools available? This will be now discussed.

Who are providing these innovations?

There is not only one path for innovation; several strategies can bring innovative solutions to a problem. Taking risk is a part of the process, a company, which always goes forward with caution, might not find anything really innovative. That is why a start-up could bring more innovation than a big company. Furthermore, there are several start-ups for one big company so it is somehow logical that they bring out more disruptive ideas. Another thing that could explain this point is that big company has already commitment for their development strategies. Be innovative naturally goes against commitment already set. It is called the immunity to change⁴⁷. To be innovative, it is crucial to identify those commitments and deal with them before setting any innovation strategy. In small companies, people are trying to make the difference compared to competitor, in other words be innovative. Because of large incomes, big companies do not have this state of mind. The strategy consists of investing a large amount of money in the R&D and work in confinement. A big company does not want its ideas to be stolen. But change has come since few years, especially with open innovation strategy.

Therefore, we can say that a start-up brings more innovation than a big pharmaceutical company. Even if this is partly true, because big companies develop innovation as well. As a matter of fact,

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Roche provides to patient new device for glycaemia monitoring that are really impressive, connected to smartphone, providing advice, etc.

As a conclusion on this short part, on one hand, we can say that a start-up brings a great number of innovations. But it is the purpose of such kind of company; if it wants to expend or get acquired by a big company it has to be innovative. On the other hand, there are two different types of big pharmaceutical companies:

- Some which remained in a standard R&D system with a great number of merge and acquisition are still providing some innovation. But this system does not seem to be sustainable and cost-effective; furthermore blockbuster strategy will not work any longer because of the development of personalized medicine. Many articles in literature say that innovative capacities of the established R&D model of the pharmaceutical industry reached their limits⁴⁶.
- The other kind of big company that really tries to develop new models of discovery with open innovation strategy. It is important not to be afraid with this new method; do not think that it will replace the R&D, R&D will be always needed. We have to see this opportunity as a support for the R&D not as a competitor.

In the light of this, let's discuss in more details the limits of the R&D system. Then, one new strategy developed, among other, within big pharmaceutical companies.

How to be innovative within a big pharma company?

Limits of the R&D system regarding innovation

Research was first an activity based on projects (for example Apollo or Golden Gate Bridge), those researches bring out innovation. But in the early 70's a second generation of R&D trend to tailor to client's need, therefore losing their innovative potential. After that a new trend consisted of a research around a problematic. As an example, we can discuss "How to treat a corn's parasite?" Starting with this problem, several possibilities can come out, such as biologic, chemical, and genetic. Thus, there was not only one project but many more. Those are now managed in portfolio of project which is at the heart of what we can call third generation of R&D⁴⁸. The third generation is still current in many companies that do not fill the gap with innovation yet.

Besides this, in many industries, there is a dominant design. For instance, no matter how a car is innovative, it is still a car. But once this dominant design disappears, the marks disappear as well (e.g., e-book compared to paper book). Then once the innovation challenges the dominant design, another form of management is needed⁴⁸. It means that big changes are needed in R&D center's management and culture, which is not easy to set in a mature company.

Moreover, in several companies, we have seen many joint-ventures that bring out bigger R&D center. However those centers are not able to sustain the competitiveness and profitability regarding competition, R&D is not a necessary creator of value in mature industry, such as pharmaceutical industry, and often constitute an overinvestment⁴⁹.

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A last thing to consider, but not least, is the immunity to change as discussed above.

Those entire things make a standard R&D centers not enough innovative than it should be. But R&D center will be always needed even if the outsourcing is taking a bigger part of the pie every day. In fact, R&D centers have to work with outsourced solutions not against, furthermore without R&D centers; outsourced solutions are not effective for the business of the company. This kind of collaboration can be set with open innovation strategy that is going to be exposed to you.

New strategy developed

A main strategy currently used to discover innovation in a field is the open innovation strategy. This has been exposed by Henry Chesbrough⁵⁰, professor at the University of Berkeley, considered as the father of open innovation. It seems important to notice that is not the only way to be innovative. As a matter of fact, innovation strategy can be set within the company but with the connectivity available between people worldwide, it is crucial to collaborate with external solutions. To be more precise, there are always more people connected on the Internet than people connected on the intranet of a company. Thus, with more brains, a solution comes out faster and might be more relevant.

The open innovation can be distinguished from the closed innovation. Closed innovation is the classical R&D system exposed above. Here are two figures for comparison between open and closed innovation⁵¹.

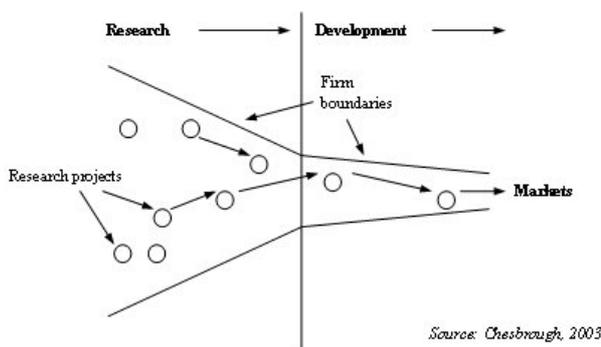


Figure 13. Closed innovation system

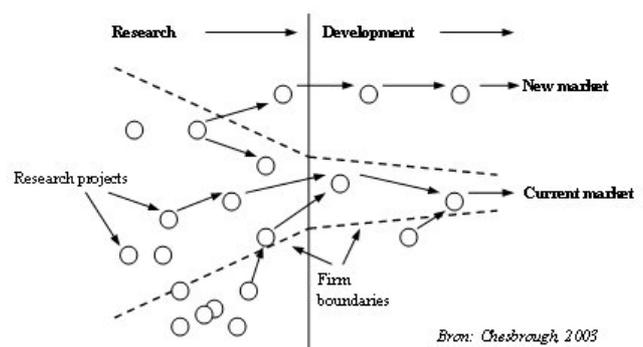


Figure 14. Open innovation system – source : h

As you can see, closed innovation is behind the firm boundaries, whereas open innovation communicates with the outside.

At the beginning open innovation took form in the way that large amount of knowledge exists outside a company. Then venture capital leads ideas and technologies to be further developed outside the company. Finally, licensing agreements enable the development of this form of innovation. As a result companies have developed other way, outside the firm boundaries, to increase the efficiency of their innovation process. Thus, open innovation can be described as: “Combining internal and external ideas as well as internal and external paths to market to advance the development of new technologies”⁵¹.

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Besides this it is important to notice that Open Innovation is a generic term for a great number of tools and techniques, the common thread is collaborates with partner and customer to develop new products and services.

Open Innovation can be a simple dropbox for customer or collaborator to submit ideas, or programs use contests to solve problems (e.g., the X-Prize). The crowdsourcing, which can be defined as the process of submitting a problem to a large number of people that used to be solved internally, is a part of Open Innovation. Transfer technology is a part of open innovation too.

At last, but not least, open innovation can be set through tools such as “Innocentive®”. It is a platform that promotes culture of innovation by sharing knowledge and solving problems. Through this, it is a network that is set between companies, making them communicate with each other, exchanging programs of development, problems and ideas. Because in every companies, many projects that are at a quiescent stage, can be useful for other companies. Through this platform those projects can find a utility.

As a conclusion, Open Innovation is a new way to think, to open the mind to others, share problems and solutions. The old system (e.g., closed innovation) does not explore the potential of tools available. It does not go fast enough. Moreover the number of people involved is limited, so is the network. Therefore, other companies, which have changed their state of mind, will surpass those which remain with closed state of mind. Open innovation is a solution to innovation’s finding. First and foremost, it has to be understood by the company and then adopted by every person within. Therefore there is a need of involvement by the top management and people below them.

As you can see, we have tried to answer these three questions about innovation (*Where, who and how*) in the aim to understand the purpose of the internship that is to “Spot, Analyze and Follow innovation”. This primary task was essential because for spotting innovation we have to understand what it is and how we can be innovative. Now let’s expose a problematic and then the solution proposed

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Problematic

There are changes in health, healthcare' system, innovative therapies, global patterns of communication between people and object. Furthermore everything goes faster every day. We see that a classical R&D system is becoming old and not always in accordance with nowadays' communication technologies. If a company wants to remain competitive, it has to evolve. Former R&D centers that can be assimilated as closed innovation are not sustainable anymore. Nevertheless, they remain crucial; the stuff that does come in from the outside rarely comes in ready to go, it is important to be able to do a lot of additional work⁵⁰. Because there is an immunity to change, it seems easier to set an open innovation solution within the company before outside the company. Even if some open innovation already exists through licensing and so on. We tried to set an innovation process finding and it has evolved as an open innovation process. Because, as it was said above, the purpose of the internship was to spot analyze and follow innovation. But spotting innovation is more relevant by setting a network and exchanging with people. Therefore, relevant problems for the company are brought out. Then spotting innovation that might solve these problems is better than spotting another innovation without real purpose for the company. This will be exposed throughout the next part.

Besides this, regarding innovation, it is crucial to notice that it is impossible to be 100% sure that an innovation will meet the expectation. This is due to several factors. The graph below, named the hype cycle characterizes very well this problem. At some time, there will be a great expectation for a new technology but before it is set on the market, much more time will be needed

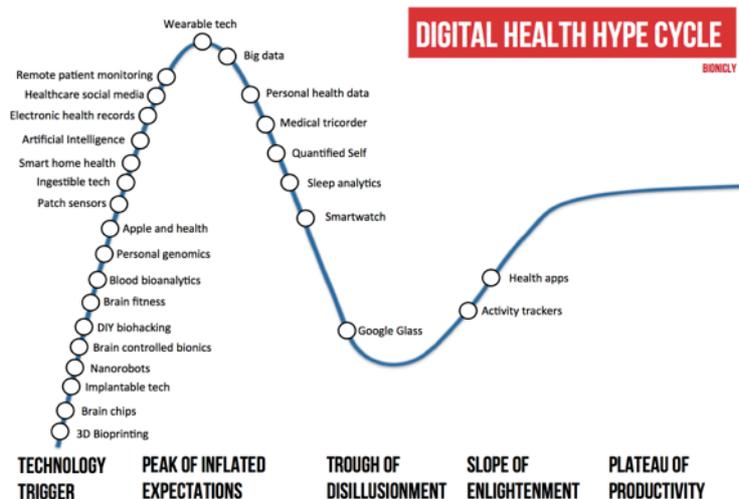


Figure 15. Digital health hype cycle – source: i

Furthermore, there is always an adoption life cycle. Indeed, it is not because something new is available that everyone will get it. It takes time too. That is why innovation comes with a long term strategy.

Now we are going to show you a process set within a company, which has the purpose to spot, analyze and follow innovation. You will see why such process comes with open innovation strategy. The first clue is that innovation cannot be carried on by a single person.

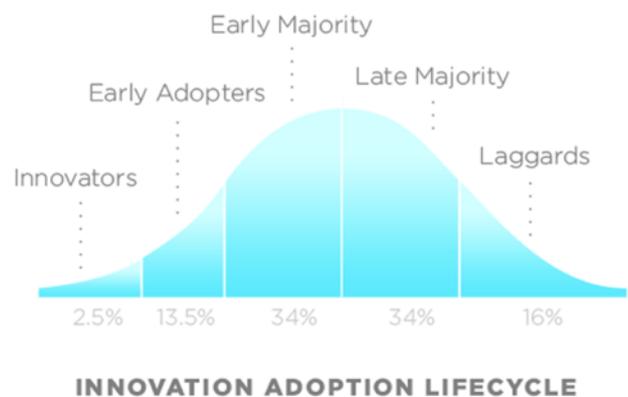


Figure 16. Innovation adoption lifecycle – source: j

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Material and method: Implementation of a process of research for innovation

Within Galderma, the mission was to set and implement an innovation process. For this purpose, three questions need to be asked:

- Where and who can provide ideas or problems?
- How is innovation investigated?
- How to share and follow innovation?

According to that, a whole process has been developed. But this process isn't frozen. Indeed, it has evolved during all the period of the internship. Starting from an idea or a problem, this innovation process is design to provide new product, device or process. This is in order to generate value for the company.

It is important to notice that some ideas of process have been developed in different units of Galderma in the past. But they were isolated and have not been implemented; they remained so. The top management has to be involved if we want a project to be achieved. To focus on the subject, the process set in Galderma is formed out of three parts. The first one concerns how to spot innovation. Therefore several paths have been tested. Then, every idea has to be investigated; a landscape about competition, scientific state-of-the-art and trend is performed. For this purpose, tools of Competitive and Scientific Intelligence, department within the Scientific Division, are used. Once the innovation is analyzed, it has to be share and follow. Those entire subjects are discussed in the followings parts.

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Workflow

On the diagram, the workflow is detailed. This is the cornerstone of development of the process.

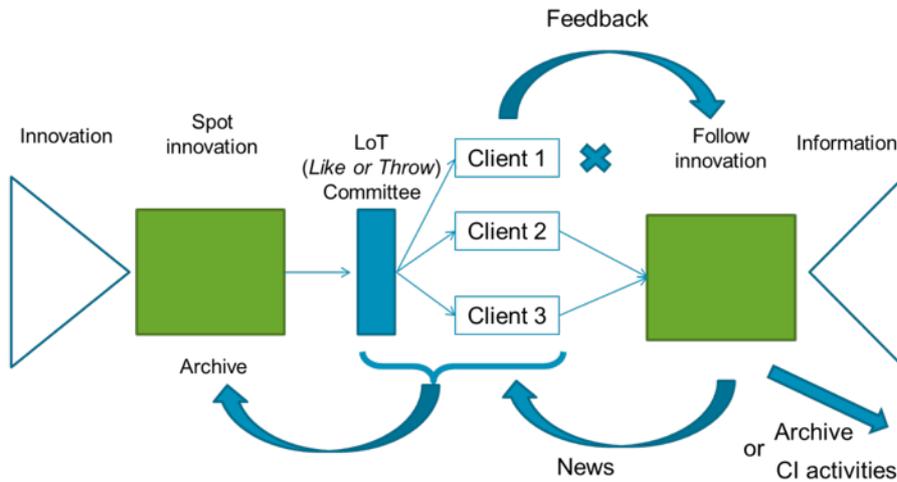


Figure 17. Workflow of the process

This process is detailed in the next paragraph, from the left to the right.

Innovation comes from everywhere; it can be news from a newsletter or found on a website. It can come from an observation made by a physician. This is even more valid for dermatologist because skin conditions remain unclear and treatments available aren't always efficient. It can also come from a discussion between two persons within the company. That's why spot innovation is a critical point in the process. Then, to do an efficient spotting, it is important to try as many paths as possible to find good ideas. That is what has been done during the internship. Another aspect that is crucial is to involve people in the project. Innovation process cannot be carried by a single person. Finally, be proactive is a keyword; spotting something on internet is good but it might be too late. On the contrary, find an innovation within the company, during a workshop, this is proactive.

Since an idea is spotted, it has to be investigated. Indeed, to support innovation research and development, a watch is necessary. This watch has to be technological, scientific and competitive. It needs to have a patent aspect as well. This last thing is too often neglected. Anyway, this is possible by using CSI tools such as Pharmaproject (database for all project in development concerning pharma companies) Orbit, which is a database for patent. Patent is a source of scientific knowledge concerning innovation that is unique. This is because inventor protects his invention through patent so it is the only document where the technology is informed. Another thing is that the trend has to be examined carefully as well. It is not because we know how to do something that this will be useful but trend can give some positioning about what is going to succeed. Trend can be observed through forum or during a discussion with Key Opinion Leader (KOL). KOL is a person that knows the trend, the needs of patient. He is also well informed about technology, procedures and innovations in the field. It can be a dermatologist or a physician or a consultant, for example.

Here was a brief summary of what can be done to investigate an innovation.

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Then, selected innovations are presented, bimonthly, to a committee formed out of people from different departments. The purpose of this committee is to select, according to their knowledge and background, the most interesting innovations that will be presented to clients. More details will be provided later.

Remaining innovations are then presented to clients. Clients can be a department that may have interest. It can be the manufacturing, the marketing, the management, etc. After that innovations are updated with news and clients feedback. The aim is to be sure that they keep an interest for it.

After a while, if the innovation does not represent an interest, it will be archived. On the contrary, if it does, it will be transferred to Competitive Intelligence's activities.

Here is the cornerstone of the project that has been set and implemented within Galderma. Of course this project was made during an internship and there are many limits to its success. This will be discussed in the part: "Results and discussion". Before that, the whole process will be presented to you. Let's start with the begin, which is to "Spot innovation"

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Spot innovation

Innovation comes from everywhere. According to this, everything has to be watched.

First of all, be informed is the most important aspect. As a matter of fact, to be aware about innovations, last technological improvement, new procedure and so on, being curious is crucial. According to this, few paths have been explored such as newsletter, participation to congress, networking with innovative people within the company. So at the beginning, we subscribed to newsletters. However, which newsletters have to be selected? If a company wants to be innovative, it has to be open-minded. That is why a wide range of newsletters has to be subscribed. *They are summarized in the table in annex 1.*

Reading newsletter every day is too much time consuming. For this reason, it has been decided to read them only twice a week. Some good information has been provided through newsletter, information concerning spotted innovations. But no innovation has been spotted with this method. However, staying informed about trend, new products and procedure is crucial for this project. Even in every work, we have to stay informed and alert about what goes around it. That is why most interesting newsletters are still consulted twice a week.

At the beginning, more than 12 newsletters were consulted, at the end, this was reduced to 8 and it was enough. However, this is not the best method to get informed about something. Do proper watches is really difficult for a single person; collaborative watch seems to be the best way to do it. This point will be analyzed later.

During the internship, there was a congress in Monaco about Connected Health. Participating in such kind of event is important. Why? You meet people involved in the field of innovation. During this congress, the main stream was an Internet of Things and wearable device. This is something that represents a lot of interest to all companies, because as we saw, it is a new way to provide care and communicate with patient. At this level, no innovations were spotted but lot of information about the trend of tomorrow health care was given;

- There are two types of data gathered with wearable device: Health data and Wellbeing data. Take one claim rather than the other will change the entire regulatory aspect.
- Monitoring the physiological parameters of a patient may induce unnecessary stress. This is not the intention of such kind of device
- Developing countries, which do not have standard healthcare system, developing their communication system such as smartphone. Because they do not have conventional communication system (such as ADSL), they build a better wireless communication system (through smartphone) than westernized countries. Therefore, developing countries trend to be ahead of us concerning ehealth and mhealth. They will represent a big part of this market.
- All giants of IT (Google, Apple, Facebook, Samsung, Microsoft...) are investing a lot in ehealth. For example, Samsung provides to Dubai a hospital ready-to-use with all the last new technologies such as Artificial Intelligence.
- Most part of the needed technology are already available, but most part of organization aren't ready for this revolution

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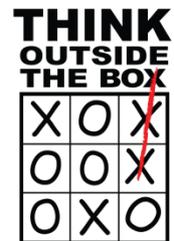
Participating to this kind of congress is really important to understand the environment and then take the good decision concerning which innovation the company should focus on.

To get informed is a main part of the research of innovation. But where innovative idea can be found?

It can be found through brainstorming within the company. To succeed, workshops have been organized. The purpose of those events was to gather people from different departments with different knowledge and give them a topic. Then, with games, we may try to identify the needs and problems of this subject and find solution.

For the first workshop, trainees within Galderma were contacted. We collected, with a form on Internet, information about present people to know in what field they can be challenged. Then a meeting is organized. During this meeting, two topics were discussed: Acne and filler. The methodology used was "Attribute listing". It is a creative technique used to find new ideas, solve problems and find innovative products and services. Attribute Listing involves breaking the problem down into smaller and smaller parts and looking at alternative solutions to these parts.

Talking about fillers, "attribute listing" lists all the components, attributes, functions and features of filler. Then we try to find an answer or alternative to these. During those events, it is essential to be creative and sometime even extravagant. The reason why is that if you want to be innovative, you have to think like no one did before. In other word, think outside the box!



Source : k

So, concerning filler, on that meeting, we designed filler formed out with Adipose Derived Stem Cell (ADSC), which were genetically modified to secrete hyaluronic acid and other compounds. Therefore, once injected in wrinkles, it will correct the aesthetical problem, and will improve the efficiency and duration of action compared to fillers available on the market. After that, an investigation is necessary to assess the feasibility of the project. Furthermore, scientific information is necessary (through publication or patent). This will be described with details in the next part.

Workshop is a good path to be innovative. But it is not enough, to improve the process, more things have to be tested and as it is written above, a support such as collaborative watch needs to be set as well.

Furthermore, an internet page has been developed to share and follow innovation. On this platform, there is also a forum, which is a good place to exchange knowledge and ideas about a topic. All topics discussed during workshop are on the forum. The idea is that everyone, everywhere, can think about the topic. At any moment one can upload a thought anywhere on a platform, it is the beginning of a collaborative watch. Through the forum, this watch is set. Then information and innovation provided on the forum can be analyzed as an innovation formulated during a workshop.

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Topics discussed on the forum are:

- Pathological model of reconstructed skin; there is a need to change the way that preclinical research is made. People are concerned about experimentation with animals, so an alternative has to be found.
- Adding a biological activity to filler: As it is known, most part of filler has only a physical property, which is to fill up wrinkles. The idea was to add a biological activity such as an antioxidant or a trigger for endogenous collagen. A crazy idea posted on the forum is to add a fluorescent particle. Thus, people can have a fluorescent face. It might be funny in a club. Some people may find this completely stupid and crazy. But the thing is some people already have implants under the skin of their faces. So it does not seem so ridiculous. Keeping in mind that foolish ideas sometimes bring more innovations than conventional ones.
- The internet of thing and wearable device; it is a wide topic. Here are presented all wearable devices that can be used for dermatology. There are discussions about smartwatch but also electronic skin tattoo. We can notice that the skin does not need to be monitored all day long. It is not like heartbeat or blood sugar. Through this forum, we have established that a single use patch will be more tailored to this application, rather than a smartwatch. Moreover, people get bored of those gadgets if there is no vital interest for them. That is why a patch seems to be more logical.
- Alternative to biopsy. As everybody knows a biopsy is a surgical act with all the constraints linked to, such as pain or anesthesia. In this way, some ideas have been proposed; for instance the use of microneedle: since it is painless, it can thus be good solution. But because of the size of the sample, following analyze cannot be too much consuming. Then we think to add to this microneedle, a lab-on-a-chip which is miniaturized and permits to have pertinent results with a very little sample.
- Skin permeation, which is a big challenge for a dermatological company. This is due to the composition of the skin and the target desired for the molecule. Here many ideas are proposed. On one side, there are many devices such as electroporation, microneedle, skin abrasion, laser permeation and so on. On the other side, we found innovative formulation like vector, liposome, etc.

As a conclusion to the forum, it is a good way to connect people everywhere. As, you never feel innovative at the right time, the forum is an alternative to express yourself everywhere any time of your day. Good ideas were provided through this forum but there were not as many people as expected, this point will be discussed later.

Through the platform, there is a last path to express your innovative idea: A live form. This form is designed to help you to give all information needed. *You can find it in annex 2.* This was inspired from Open innovation platform of big pharma company. But it does not meet the success expected. Like the forum or the workshop, we will see that the limits are quite the same.

The last way to spot innovation is the discussion with people and moreover the networking between them. On one hand, there are people with problem, but with no solutions. On the other hand, people with an idea but no applications. Put them together and then you get an innovation: Innovation is when a problem meets an idea. During the internship most innovative ideas were provided through

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discussion with a person. Within Galderma, we spend a lot of time to meet people, to understand what they do, what is their environment, what are their problems and solutions. Thus, we had idea or a direction to seek to be innovative. Sometime, people bring us the innovation and then we just had to investigate the feasibility.

As a matter of fact, during the internship, three missions were submitted as innovation's scouting:

- First one was from the packaging, which asks three questions: What is the packaging innovation for? What is packaging innovation for you? What is the last packaging innovation you have seen? As a response, we provide them a document of few pages with the trends of tomorrow's packaging followed by a presentation with several slides describing methodology for research of innovation and how to identifying the needs that a pack can answer and so on.
- Secondly, a request for a landscape on bispecific antibodies was made by a manager. Therefore, we made an overview of more than 40 companies with almost 110 molecules under development. An ad-hoc analysis was done and shared to several managers. We describe bispecific strategy compared to classical mAb, each technology with its advantages and drawback, the main indications of these products etc. *An extract is available in annex 3.*
- Last, formulation department asked for a landscape regarding liquid patch. Thus a scouting of some players was performed through company's website analyze and patent landscaping. The work was discussed during a meeting with client.

These works are not directly a part of the process. But since someone was dedicated to innovation within the company, people knew that he can provide a landscaping on a specific technology. This is totally the purpose of the mission which is to spot innovation. This was possible only because of the network built ahead.

As it is shown, few paths have been assessed to spot innovation. Spotting innovation cannot be done alone. There is a real need to connect people together. It is the same with computer, three computers work better than one. Therefore, a collaborative watch has been tested through forum and workshop. However, it does not work as well as expected. It will be discussed after. Now, let's talk about analyses performed to assess innovation. All the tools used will be described with a short summary of their advantages and drawbacks.

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Analyze

All analyzes performed were based on Competitive Intelligence's activities, which are:

- Scientific landscape based on publication and patent
- Competitive landscape based on press release, database of project, clinical trial, basic search on company's website.

From this, the analyst gathers a maximum of information and makes a sort of pruning with it, so that to keep only the most attractive one. Then, he gives some suggestion about the way for strategic and tactical decision to be taken about the innovation. It also enables to minimizing the risk of a project. Actually, if there are already many companies that work on an innovative technology, go on it will not add a great value. Furthermore competitor may be more advanced on the topic then it will be harder to fill the gap.

Because of this, analyst is crucial; from the amount of big data gathered, he will provide real value for actionable intelligence. It is like a distillation process that gives the right information for the right client.

Now, concerning innovation, applying those analyses is not as simple as it seems. This is due to the fact that CI's activities are made for analyzing drug or device developments. As we know, innovation may come from everywhere; it is not possible to make a survey about a smartwatch in the same way that a survey about psoriasis treatment is done.

All tools used for analyzing innovations are listed below:

Publication: Scopus, PubMed

Patent landscaping: PatentInspiration, Orbit, Innography

Drug development: Pharmaproject, Mintel

Clinical trial: clinicaltrial.gov, trialsearch WHO

Internet: Company website, google search, press release

If a methodology can be set for this work, here are the highlights. Keeping in mind that the methodology is not static; in fact, it adapts for each innovation.

First, starting from an idea, a review of publication is performed to gather a maximum of information about the technology. The research is performed with keywords. It is however hard to identify all the synonyms. This is even more important for patent search because applicators try to hide their patents through synonyms to avoid industrial spying. It will be exposed further down.

As an example, one spotted innovation is the plasma technology used for medicinal purpose. This technology is also known as the fourth state of matter. It has been developed by NASA in the 70's; the flame produced through plasma technology is cold. That permits a great number of applications such as sterilization of the skin, reducing the wrinkles or disinfection of wound. To learn more about this innovation, a research has been made on publications. Keywords and synonym have been

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identified: Plasma technology can also be named as cold plasma, non-thermic plasma or atmospheric pressure plasma. If a research was made with only “plasma”, a thousand of non-related articles (e.g. blood plasma) will pollute the results. That is why identifying all synonyms is important; to be sure that we do not miss any article that speaks of the innovation. It is also important to make sure the noise is not too loud.

Then the application has to be identified as well. Here it is the dermatological application that we are looking for. So it is exactly the same as the technology, all synonyms have to be identified: Dermatological, Skin, Derma, Topical, etc...

Once synonyms are identified, we build an equation of research by using Boolean operator (AND; OR; NOT) plus some other operator like:

- Proximity operator: It permits to search two or more words one next to others. As example searching “Plasma technology” has to be written: Plasma NEAR/2 technology. That means the word “plasma” is two words far from the word “technology”. The way to write these operators may vary from a database to another
- Truncation operator: It permits to research several terms, or if we are not sure of the exact word spelling. Most part of the time this operator referred to with a sign a “+” or “*”. For example, if we write Derm+, results will be for derma, dermatological, dermatologist, dermatitis and so one

There are a great number of operators, which can be different for each database. However knowing Boolean, proximity and truncation is enough for basic research.

To summarize about search’s equation, three important compounds have been identified and have to be used for a good research:

- The technology
- The application(s)
- The operators

It is important to break down the equation. First one is to search the technology (with all synonyms). Then a second one is performed for applications. This will permit to be sure that we do not miss anything during the research. The more we break down the equation, the more accurate we are.

Some publication databases have thesaurus, like PubMed, this enables to select terms related to articles. Every articles uploaded on the database is reviewed by a person that sets different terms according to the publication. Then, when we perform a research through the thesaurus, with those term we will find all articles related. This is good for “application” research. Skin, for instance, is a term that can be found in the thesaurus.

After these explanations, we can write the equation of research for the plasma technology applicable to skin condition. For PubMed, it is easy because, through the thesaurus, terms “skin” and “plasma gases” are available. The equation looks like: (***"Skin"[Mesh]***) AND (***"Plasma Gases"[Majr]***). We will see that for patent, research is more complicated due to the different fields available (e.g. title, abstract, claims, etc.).

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Concerning research on publication, 15 articles were found. Thus, we can identify:

- Some players: Who is developing this technology?
- Some technology used: What kind of gas is used?
- Some applications: Is that for wound healing or aesthetic purpose?
- The trend: How many articles are written per year?

Then, we use Orbit for patent landscaping. As we said earlier, most part of technological knowledge is present only into a patent. The methodology of research is the same except that the fields need to be selected. Using different synonyms plus research operator, the equation looks like: ***((skin OR derm+ OR topic)/TI/AB/IW/CLMS/OBJ/ADB AND ((cold OR atmosph+ OR (no+ 2M therm+)) 2M plasma)/TI/AB/IW/CLMS/OBJ/ADB) AND (EPRD >= 2010-01-01)***

Breaking down this equation is as follow:

- The technology: Cold plasma OR atmospheric plasma OR non-thermal plasma. 2M is the proximity operator
- The application: Skin OR dermal OR topic
- EPRD is the date of priority. This permits to skip old patents. Here we choose 2010

With this equation, 88 family of patent have been identified. A family of patent can be defined as all patents submitted on a national worldwide level, which protects one invention.

Through patent, players are identified. Furthermore, patent databases have analytic tools that permit to have an overview of competitors, technologies used, etc... That hastens up the analysis.

We can notice that these databases have something they call “Innovation tools” that will allow, from a pool of patent, to identify the needs, the attributes and other things related to the technology. Thus, we can found innovation for this technology. Methodology is provided on their website. It is a good path to spot some innovation. It has also been tried during the internship, but it easier for an expert in his field (e.g. a researcher in chemistry) to use this kind of tool to be innovative.

After the patent landscaping, four players have been identified. To know their advancement in the development for medicinal purpose of this technology, few researches are performed on clinical trials.

Indeed, some trials have been done with plasma technology. The methodology of research remains the same with operators and keywords. According to the phase (I, II or III), it is possible to determine the launching date.

A last research, concerning the plasma technology, is to go to one company website to gather more information. It is important to notice that on these websites, information provided is always favorable to the company... To be critical with that information is crucial.

After gathering all information from those databases, the analyst’s work just began. The aim of the analyst is to identify the main players, the opportunity for licensing, merging and acquisition, etc. Roughly speaking, after the analysis, a report is made with:

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- Description of the idea / innovation / technology
- Application for our business
- Competitor landscaping
- Patent landscaping
- Clinical trial ongoing (if any)
- Some advice made by the analyst

All reports made about innovation during the internship were approximately identical to this one.

Once the innovation is analyzed, it has to be presented to a committee for a selection and then it will be presented to client. This is what we are going to expose in the next part.

Share and follow

Once the innovation is spotted and analyzed, it has to be shared, first to a committee for a selection and then to clients.

The committee that was called “Like or Throw Committee” is composed of people from different departments: Licensing, Competitive Intelligence, Industrial property, Scientific Information, Formulation, Early development, Pharmacology in vitro, Structural Biology... Because of its plurality, this committee can select innovations with relevance. Innovations are presented through a presentation form, which is very simple (*See the annex 4 for an example of this form*), people from the committee just have to click if they like it or not. They can add comments as well. Then, they just send it back to the service for analysis. If an idea has more than 75% of “like” rather than “throw”, it will be selected and then presented to clients.

Then, how to present innovation to clients that are dispatched worldwide? An internet platform appears to be the best solution for several reasons:

- It is easier to share with clients. Email is not the solution for people who received more than 150 mails a day. It has to be a relaxing time too when we share to them innovation because people have already lot of work to do. To load them is not interesting so we are trying to find a pleasant way for them to be aware of innovation
- It allows to gather different parts of the process: Shared innovation and forum
- We can add information about innovation without sending a new version of a report by mail
- A “news” page was added to inspire visitors, trying to make them think about a problem
- Add an innovation form, which allows everyone to submit an idea
- Because the revolution is digital and to be effective we have to use the most innovative tools. Email was innovative 15 years ago, but nowadays, it is essential to try new ways of communication

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The platform was built through SharePoint, which is a tool developed by Microsoft. It enables anyone, who has some clues with IT, to make his own. This platform is composed of 6 main parts:

- **Home page** gives information about what is going on (e.g. the dates of workshop are provided); there is also a link toward the other pages. An excel sheet is presented but only reachable by the team in charge. On this sheet, all innovations are listed, even if they will not be analyzed. Thus, no information is lost.
- **About:** This page is here to explain how the process is made. Some presentations, webinars or reviews about innovation in dermatology are available as well.
- **News:** Twice a week, most interesting news gathered through newsletters are posted. Thus, we try to inspire people to be innovative
- **Forum:** As presented before, the aim of this forum is to deal with topics that are full of interests for the company.
- **Innovation:** Here are gathered all innovations spotted, with an analysis per innovation, some information, etc... There is a possibility, through a form, to give feedback. This allows knowing what innovation is full of interest and which is not.
- **“Share your idea”** is a form made to help people to submit their idea. It is important to notice that lot of big pharma is developing those kind of forms, which are available on Internet. Therefore, anyone can bring his idea. This is what we call “crowd sourcing”. It is very trendy.

This platform is named “Open Innovation” platform, because the purpose is to connect people, make them do a collaborative watch about topics. If they exchange about problems and solutions, they will be able to find innovation. *Snapshot of the website are available in annex 5.*

Most part of the work made during the internship is available on the platform. As we will discuss later, it was a good idea but it did not work as well as it was expected.

To sum it up, we have seen several ways to spot innovation and then the tools used to analyze it. Once it has been done, most interesting ones are presented to the “Like or Throw committee”. This committee selected once again. After, innovations spotted, analyzed and selected are uploaded on the platform. Therefore, they will be available for consultation by clients. Furthermore, news and information concerning these innovations are uploaded to be aware of what is going on. We really tried to set a collaborative watch, to increasing the relevancy of information and be sure not to miss one.

Here is the whole process of “Spot, analyze and follow innovation” but there are many limits to the smooth progress of it. However, about 8 innovations were spotted and analyzed during the internship. Then 6 were selected and uploaded on the platform

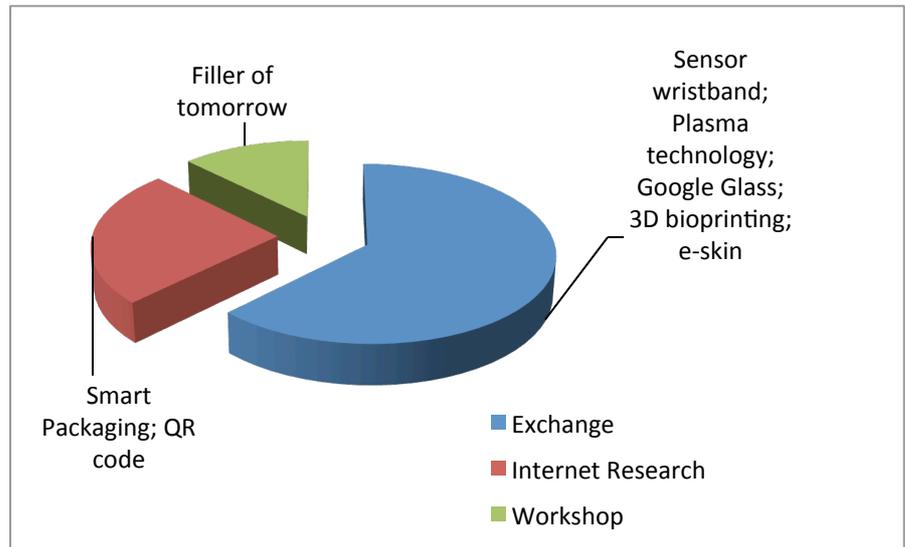
Besides spotted innovation, advantages and limits of such kind of process will be exposed in the next part.

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Results and discussions

Now that the process has been exposed, we will see what innovations have been spotted, analyzed and shared. We can notice that those innovations have all a dermatological applications. Most part of ideas was found through exchange between people, not by reading newsletters.

As we can see on the graph below, concerning the eight innovations spotted during the internship, most part was during an exchange with one within the company. However, the filler of tomorrow was spotted during the workshop. Indeed, the team has identified the needs of an aging skin. Then it tried to found a solution for all



these requirements and gives an innovative product as filler. It will be exposed further down.

Even if it is not the best way to spot innovation, Internet research allows finding some. But to identify the needs it is better to be a team that works on the subject rather than one person. As it was said several times: Innovation is a process that cannot be carried out by a single person.

Now let's have a look at these spotted innovations one after the other. It is important to notice that these innovations have already been selected among almost 50 ideas generated. Those have been spotted through exchange, Internet research or workshop. It is useless to present fifteen innovations per month otherwise clients will get bored and will stop following us. That's why we decided to present up to six innovations bimonthly not more.

Sensor wristband:

Originator: During an exchange with someone within the company, he exposed us that self-monitoring was one of the pillars of tomorrow healthcare. It seems to be logical that skin has to be monitored as well. Starting from this idea, some researches were performed on Internet.



Source : I

Description: It is a wearable device that measures your skin moisture, sun exposure, even more, the environment around (e.g. air pollution). The aim is to control skin parameters to respond to the needs of it according to the environment.

Application: Using this kind of device can allows protecting skin health capital. As a matter of fact, sun exposure has to be monitored. Too many people put sunscreen only once or twice during a day under the sun.

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Advantages: This device really improves the customer's experience. The patient is able to know how to protect his skin, what kind of product he should use on a summer sunny day or under a particular polluted day and so on.

Limits: As in most part of wearable devices that are "well-being" device rather than health device (e.g. respectively activity tracker vs. pacemaker), users get quickly annoyed. As a matter of fact, three months is the period of using before get bored. It can even be more true for the skin, except for sun exposure, the skin does not need to be monitored 24/7. Monitor once a week can be solution. Patches can be a clue as we will see with the e-skin.

Another problem is the accuracy of measurement. As it has been observed with smartwatch, the technology is present but the accuracy not yet. Imagine that this device monitor the sun exposure linked to a treatment. If the accuracy is not good enough, some adverse effects may come out

Conclusion: This innovation is truly one that will find its place in the skin health management. For now, the form it would take is not sure: will it be sensors integrated in every smartwatch? Or will it be a single use patch applicable from time to time to know our skin condition? One says that accuracy is the problem that has to be fixed.

Concerning the analyzing, some players, focused on dermatology, were identified. For example, there is one company that develops sun exposure sensor. This device communicates with your smartphone to alert you when you need to put on sunscreen. It also permits to measure your rate of D vitamin synthesis. However there are not a large number of players. Will big companies that develop smartwatch such a Google, Apple, Samsung, take the entire market share? Will dermatological companies try to develop their own device or even watch? Nothing is sure yet but this innovation has to be shared and followed.

Plasma technology

Originator: This idea was given by a manager who read an article about this during a flight for work purposes.



Description: Active plasma components, such as molecules, atoms, ions, electrons and photons, reactive species, ultraviolet radiation, optical and infrared emission and heat have the ability of activating, controlling and catalyzing reactions and complex biochemical procedures.

Application: Sterilization and disinfection for wound healing or disease induce by microorganism such as Acne. It can blast away fine line and wrinkles on the surface of the skin

Advantage: Through publication, this technology claims that it is harmless compared to laser therapy.

Limits: Currently, miniaturization of material is a big problem. Also there is also a need to train practitioner.

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Conclusion: This innovation can bring a breakthrough in the way that wrinkles and scars are treated. It also enables a sterilization of the skin without too much pain. It is a well-known technology developed in the 70's by the NASA. The sterilization at an industrial level widely uses this technology. There are only few clinical trials that have been performed since few years. The purposes were sterilization of skin, onychomycosis treatment, dental restoration and decays prevention. Furthermore, through press release, there seems to be a growing interest for aesthetic purpose. So, we can say that this innovation shows a great number of applications in dermatology and should be followed.

Quick Response (QR) code



Originator: This idea was imagined as a response to the following question: How can we improve the information provided to customer through the packaging? It has to be on the packaging; it does not have to be expensive and must be read through digital support (e.g. smartphone). This question is already answered by agribusiness companies. Indeed, some have added a QR code, which can contain a lot of information intended for customer, such as origin of the product, link toward a short video, and so on.

Description: QR code is a two dimensional code, thus it can contain much more information than a standard bar code. Moreover, adding a special ink can make the code change if there is a contamination of the product. Thus, customer can be advised of this while he scans his product.

Application: Add this to product can increase its safety, it can also allow a better tracking. We can provide to the customer an original and interesting way to get informed about his product and the best way to use it. It sounds better than a standard notice.

Advantage: There are a great number of advantages. First, it is really cost-effective. Secondly, the customer will enjoy that more information is available for him. It will increase the confidence between him and the company. It will also reduce the risk of counterfeiting. As each code can be unique when scanned through an application provided by the company, one may know whether it is true or false. Finally, when a customer scans this code, the company can be informed where its products are used and by whom. So the sales strategy can be improved. This is a part of the Customer Relationship Management.

Limits: Like every strategy against counterfeiting, this one may crack. There is also a need to use a camera to scan the code. By adding ink that reacts to the presence of contamination is quite expensive up to now.

Conclusion: As it starts to be widely used for food and beverages, this technology should be used for pharmaceutical products. The mere reason is: it will provide a great number of information to the customer. Therefore, he will enjoy knowing the origin of his product and so on. And finally, the relation between a company and its customer will be improved. Another aspect is that the product will communicate with the smartphone. Thus, it will be connected, which is important in a world that trends to connect everything together. Even if there are some limits, this technology is priceless, so it shows many interests.

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Google glass for Aesthetic & Corrective purpose

Originator: This idea was given by a researcher within the company because of a problem met by plastic surgeons. Indeed, when filler is injected, the syringe should not touch the vessels. To avoid pain and bruises for the patient, and also vessels deterioration, the physician must see them while is making his operation.



Source : n

Description: A technology using an infrared light (or ultrasound technology) enables the uncovering of vessels' network. It is already used in North America by the nurse before taking a blood sample. Adding this technology to Google glass will permit the vision of vessels directly in front the eyes. That is called increased reality.

Application: Provide a tool of increased reality, which allows the doctor to uncover vessels, enables a safer use of filler.

Advantage: Glasses equipped with this technology is already available for nurses. The technology is well-known and not so expensive.

Limits: Accuracy of the image provided has to be improved: vessels' network of the face is finer than the one of the arm and therefore a better image is needed. Some alternative devices, such as microneedle, are in development for filler administration. We can then ask ourselves if developing this technology will be useful tomorrow. As we already said, it is not because a technology is developed that it will find its place.

Conclusion: Increasing reality to assist doctor during his work is full of interest. Indeed, it will improve every technics by reducing the risk of adverse event. However, it is important to assess the requirement of physician: Will they need it? Will it be needed as long as the devices will change? To conclude, this technology is attractive but his future in this application remains unpredictable. *This innovation has not been held for the rest of the process.*

Smart packaging – Smart Caps

Originator: Through internet research, this innovation has been spotted. It is developed by a small company located in USA.



Source : o

Description: This technology using RFID technology has been developed to improve compliance of patient. As it has been describe above, smart packaging has a great number of innovations, this one is focused only on compliance. Each time the cap is open, a signal is transmitted to the smartphone. Therefore it would be of paramount important to the patient with mental disorders in case he forgets his medicine. The cap can be automatically locked to avoid any overdose. On the contrary, a notification can be sending on the smartphone if the patient misses his intake.

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Application: Add this technology to cream and lotion's packaging seems to be logical. The application is the same as for mental disorders: Improving the compliance of the patient, avoid overdose and missed intakes.

Advantage: First, this technology will improve the compliance of patient; therefore it will improve the efficiency of treatment while adverse events may decrease. Then, we can easily add temperature sensors as well as a hygrometric one, thus monitoring storage condition will improve the safety of the product. Many other applications can be imagined as a smart packaging.

Limits: Currently, cost can be a limit but it will decrease as soon as this technology becomes ubiquitous. Another aspect is the regulatory issue, indeed, if a technology tells the patient when he has to take his medicine, it has to be flawless.

Conclusion: This technology will be available in most part of tomorrow's medicine. In the context of connectivity, everything trends to be connected. It is normal that our drugs will be connected as well. It will improve the safety of the product as well as the compliance. Thus, it will increase the value of drugs' efficiency. It is essential for treatment of mental disorders but treatment for elderly people as well. *This innovation has not been held for the rest of the process.*

3D bio printing

Originator: After a discussion with a biologist, we identified one big need: For preclinical research, we need to have pathological models of skin that live more than 3 weeks to observe a potential effect of drug candidate. The use of a 3D printer for creating models of pathological skin could be a solution. [Source : p](#)



Description: 3D bio printing is based on a simple concept: Add different layers of different cells on a scaffold. Then some growing factors are added, therefore the neo organelle starts to grow to provide an organ such as skin or liver in a short time.

Application: When the skin is built, pathological cells can be added. Thus, we can get pathological models to experiment different drugs.

Advantage: There are several advantages to use those models: (1) no more animals or skin's donor for preclinical trial, (2) the duration of time of skin will be drastically improved, (3) we will be able to choose each skin conditions to be as much relevant as we can, (4) because skin is human derived it will avoid immunogenicity problems.

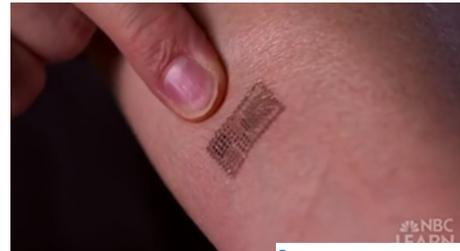
Limits: Nowadays, this technology is still under development. There are not many players, moreover only one big competitor can provide approximately a functional liver. Furthermore, all properties and functions of the organ cannot be reproduced.

Conclusion: Even if there remain some limits as it is cited above, the technology shows lot of promises. It will enable to process relevant preclinical trial for the testing of drug candidate. Moreover it will stop polemics about animal's testing.

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Artificial electronic skin:

Originator: Through discussion with a researcher in early development about sensors such as sensors wristband, the fact that monitoring the skin 24/7 is useless appears. Indeed, unlike heartbeat, skin does not need to be watched continuously.



Source : q

Description: Thanks to nanotechnology, sensors can be now micronized as small as a skin tattoo. A Bluetooth chip can be added, therefore the patch communicates with a smartphone and then gives all information about measured parameters. Furthermore, adding microneedles to this device enables to measure body parameter. There is already underdevelopment this kind of patch that measure glycaemia and insulin.

Application: Use this kind of device enables a monitoring of the skin. Therefore we will be able to preserve our health capital. If we know when the skin is too dry or too much exposed under the sun, we can easily react in consequences.

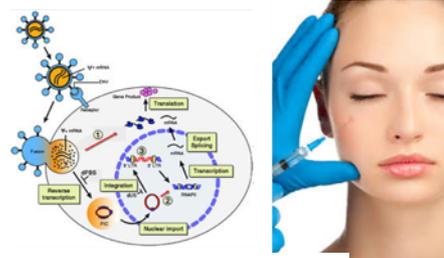
Advantage: On the contrary of sensors wristband, which remains an interesting innovation, this device is much more understated. Furthermore this patch will be a single use patch, so if the patient does not want to use it anymore, he just has to stop buying new ones.

Limits: There are some problems such as communication with other device, battery's issues or the cost of the technology. But as it develops, these problems will be solved by mass manufacturing.

Conclusion: This small device will enable anyone to monitor his skin either in pathological or healthy conditions. As it is a single use patch, there are no financial issues like buying a wristband without being sure that is useful for us. Even if there are some limits, it seems to be the best way to monitor parameters (skin and body) in a discreet way.

Filler of tomorrow:

Originator: This innovation is totally fictional in the way that there is no development of it. But different parts of this conception already exist. So the fantasy might become real. During the workshop in April as described above, we imagine a filler formed out of Adipocyte Derived Stem Cells.



Source : r

Description: First, cells are picked up on patient. Then, cells are genetically modified with a lentivirus; therefore they will secrete active substances such as hyaluronic acid, antioxidant, or why not a perfume.

Application: This can be a new therapy that will preserve skin health and reduce the time's effect. Skin aspect truly has social impacts. Furthermore, with medicine improvement in the coming decades, we can expect to have a longer life. To keep a healthy skin will enable us to look 40 years olds at the age of 60. This method will last more than common filler currently used.

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Advantage: This product will have an increased duration of time. Many biologicals functions can be added and personalized for each patient. Furthermore, to use patient own cells will avoid immunogenicity issues.

Limits: Different step of the process have been identified but the whole process does not exist yet. So it is still fantasy today. Furthermore a story of adverse event was reported, few years ago a patient received ADSC as fat graft in wrinkle. Few months after the operation, she told her surgeon that every time she was blinking there was a sound. After, analyze disclose that stem cell has differentiate in bone... Then a bone has grown just next to the eye! It shows another limit of such kind of therapy.

Conclusion: There are some patents that show stem cell's uses for aesthetic purpose. Moreover, there is lot of concern about cell therapy. So imagine this kind of product has interest. Companies that develop these technologies should be followed because if it is launched one day, stem cell therapy for aesthetic purpose will be a real breakthrough.

Those entire innovations presented are in the scope of dermatology and can represent a real interest for Galderma. As a matter of proof, many companies are developing that kind of technology for dermatological purpose. The process of spotting innovation seems to work, even if all innovations might not be spotted, the one spotted are relevant. It is crucial to exchange with people within and outside the company. Therefore, needs can be identified and spotted innovation are more relevant than the one found throughout internet research.

Here are the innovations spotted and followed during the internship. Now let's discuss about analyzes' advantage and drawbacks.

Analyze:

The tools provided within the competitive intelligence of the company were developed for drug's watch more than device or technology. But the bases remain the same: Watch patent, publication, press release, company's website and, if it is possible, clinical trials.

The advantages are that CI provides expensive software where analytical tools are already available. Through patent and publication we can find competitors that work on a technology. Being in a big company enables to order articles, which is better than only read free ones or abstracts only.

Concerning limits, databases provided within Galderma are made for drugs such as Pharmaproject. As seen before, this tool summarize most part of what needs to be known during the development, therefore launching date can be determined. As well as directions taken by companies; do they develop more for psoriasis or rosacea? This kind of question can be answered. Regarding innovation, it is quite complicated. Indeed, patent can provide answer about technologies, direction taken by company. But no lot of news about strategy, launching date and so on.

There is a big need to determine which tools are useful for innovation's analysis. As a conclusion, analysis can be performed, first through patent and publication to establish the state of the art and competitive landscape. Then, we can watch clinical trial to make an idea of the launching date. But

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this will not be available for all innovation (e.g. smartwatch does not required clinical trial so far). Analyzing innovation is a process difficult to standardize.

Like or throw committee:

The first committee was made during April, 5 innovations were presented to 7 persons. 5 responses were gathered through email plus one while speaking with one person. This shows already a limit of this process. Even if the presentation was concise and easy to respond, it is already too much time consuming.

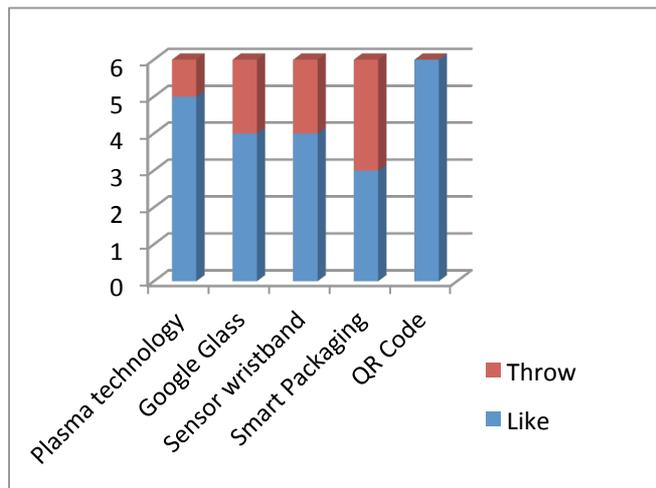


Table 3. Results of the first LoT committee

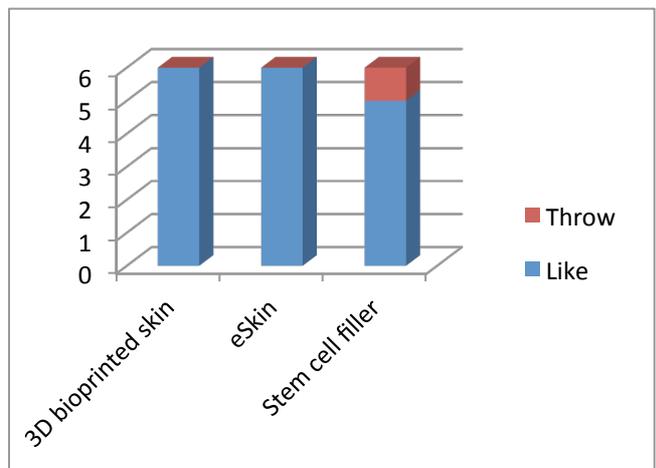


Table 2. Results of the second LoT committee

As we can see on the graph, everyone liked the QR code. This innovation was then uploaded on the platform as well as plasma technology. Besides these ideas, a choice was made between Google glass and sensor wristband. We decided to choose sensor wristband because, as a part of the internet of thing, it is sure that it is a technology to follow. Furthermore, as discussed above, Google glass might not find its place as a support for filler administration. This is due to the fact that a needle might not be used anymore so there will be no need to uncovering vessels' network.

So three technologies were selected and uploaded on the platform to be shared and followed.

For the second committee, which took part in July, 3 innovations were exposed to 7 persons. Among six responses gathered, three were by email and three others were through speech. One person did not have time to respond. Nevertheless, six responses are enough for the process.

As you can see, spotted innovations were presented the “Like or Throw” Committee. From the first committee, 3 innovations were uploaded on the platform. From the second one, all innovations were kept then uploaded on the website.

Why this committee is really important? Because one has to be sure of the relevance of spotted innovation. Indeed, people belonging to this group are expert in their field, therefore their opinions are good. However it can be difficult to get their feedback because of their busy schedule.

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Furthermore, the number of people is restricted; to get a better idea of the interest of an innovation, it should have to be presented to a larger number of collaborators.

As referred above, the purpose of this committee is to make a relevant selection of interesting innovation that should be followed. But keep people motivated is rather hard. Maybe innovations should be uploaded at an earlier stage on the platform. Then everyone, within the company, can give his opinion and information about the technology.

As an example of limit, when we presented the “3D bioprinted skin”, the analysis did not find any competitors. However, once presented to the committee, through feedback, competitors were identified. Besides this, one who took part in the workshop, send us the same information (just after the publication). This is why, if the innovation is uploaded and a collaborative watch is set, this kind of mistake can be avoided.

To conclude on LoT committee, this is a crucial step in the process but presenting this to a larger number of people might be better for the relevance. Furthermore, another way of presentation (other than presentation form sent by mail) has to be designed. And an involvement of top management within the company is crucial if we want this process to work. Indeed, people have immunity to change and ask them to be a part of this process is hard when there are no actions from the top management.

Internet platform:

Regarding the platform, it is a good tool for share the information. Rather than email, which can be lost among daily arrivals, this website allows the user to get the information that he is interested in. Furthermore it is an alternative path for share ideas and problems about a topic. The purpose of this platform was to put people together; therefore they can be time-efficient for solving problems, share ideas and so on. It was also designed to set a collaborative watch. Then, we are sure that we do not miss anything important among the entire data published every day on Internet.

Theoretically, the concept is great and awesome at the same time: Everybody is linked together, sharing ideas, problems and news that lead to innovation. Furthermore it is a support to the process: Spot, share and follow innovation can be made from the website.

The reality is that it does not work as well as expected. Indeed, only few people went to the platform to share ideas and problems. Moreover, even if some people posted information to follow innovation, they did this around the workshop but this stopped once the event past.

The purpose of the internship was to set a process for “spot, analyze and follow innovation” but many limits have been identified. Anyway, setting this platform was not purposeless. On the contrary, it proposed an alternative to email, which is definitely no more a solution to communicate within a company. It seems important to notice that companies which make innovation’s research develop this kind of platform. Some others have “enterprise social network” for all exchange not only dedicated to innovation, therefore communication between people can be made everywhere at any time. That increases the speed of all project development and should be adopted within the company.

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As a matter of fact, communication between people has developed in the following way: A 25 years old boy, when he was 11 he used to exchange through email with his friend. Then, when he was 15, he used messenger. After this, social network appears when he was 19. Therefore, social networks are the best way to communicate, make event, share project and so one and so forth. That is why it seems logical that communication, within a company, has to switch to a company social network. Nowadays, mail and messenger are not enough to be efficient.

The process:

To discuss about the whole process, there have been two phases in this project. The first one was to find innovation through internet researches, which we can call "*passive search*". Then, the second one was totally devoted to connect people together and find innovative ideas through exchange. It can be named "*active search*". This methodology is more relevant; company's requirement can be identified. Moreover, with active search, innovation is supported by several persons rather than one.

As parts of the active search, works made outside of the process are ad-hoc analysis (e.g., innovation in packaging, landscape on bispecific antibodies and landscape on liquid patch) were full of interests. Those works were asked and then performed only because of the network set during the internship. It is one extra example that networking is crucial for innovation finding.

Some parts of the process were disregarded: The dropbox and the forum did not work because not enough people were involved but these strategies are important regarding innovation and have to be set for next process. Indeed dropbox helps people to be innovative and allows anybody to bring out its ideas. Innovation comes from everywhere. Besides this, forum is crucial if we want to set a collaborative watch.

A weak point of the process is the analysis part. Indeed, expectations have to be clarified; some improvement can be done such as:

- Added value bring by the innovation for the company
- Business plan and strategy required for the development of an innovation
- Customer's needs regarding this technology

Now that results were exposed and discussed, let's conclude.

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Conclusion

First of all, as a recap of what has been done, we can say that:

- A whole process has been set and implemented
- Active search was preferred to passive search
- Some parts of the process were eliminated because there were not enough resources to make them work
- Analyzing part need to be improved
- 6 opportunities were finally presented after the process selection. Those innovations seem to be relevant for a dermatological company
- Three ad-hoc analysis were performed for three different departments, this was possible only because of the network set during the internship

Following this, several recommendations can be highlighted. The most important thing is that resource allocation is necessary. Man and materials are required if such kind of process is implemented.

Regarding organization, we have to put a coordinator to make it run. Indeed a coordinator is the link between people. Moreover he can play the role of administrator on the website. Since a person is dedicated to innovation and people within the company are aware of that, it become easier for everyone to ask him as soon as they have a request regarding innovation. After that, the coordinator can redirect to someone more specialized. The coordinator is a crucial part of the network. Concerning materials, the platform through SharePoint shows many limits. If we want the process to be tailored to the company, it is important to be able to do anything and adapt it as the process evolves. Therefore, an Internet page is needed. Besides this, if we want to make good workshops, materials might be required too; the aim is to stimulate people. Anyway, there no big needs of materials, man remains above everything.

Then, once we have resources, it is crucial to set a sustainable network within the company. As we see a weakness within classical R&D centers is the lack of communication within and without the company. Therefore, the main mission of a person should be to create a network. Starting with these, people will communicate more, project should go faster.

Speaking about technologies available, we know that we can approximately do everything we want. As a matter of fact, it is possible to monitor every route of administration, through patches, smart pills, nanorobots and so on. The most important is to determine what we want to do, where the company wants to go. The real question is not “how we can do” but “what we want to do”.

As we discussed above, every change goes against commitment already set. Therefore it is crucial to identify those commitments and then try to be innovative while considering them. Furthermore there is a big requirement; management needs to be involved in the innovative strategy. Otherwise, nothing is really going to move forward. People are divided in several categories (e.g., innovator, early adopter, early majority, late majority, laggard). Therefore not everybody will naturally adopt a new strategy. Then, manager can take action and show benefit of it to his crew. Innovation process

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needs to be accepted by the whole company because it is a state of mind and this process needs support from each person. This is a crucial point. Furthermore in a big company its existing for decades, the challenge is bigger than in a small company, because we have to convince all collaborators.

To conclude on this paper, be proactive is a major issue. Therefore scouting innovation without a direction given is useless. On the contrary, when a thematic was given (e.g., bi specific antibodies), scouting innovation takes sense but it is not the only thing. To have the ability to innovate and propose the right solution, scouting innovation might not be the solution. Instead, be innovative within the company, by using methodology (e.g., open innovation platform, workshop, collaborative watch) might be more relevant. In any case, it is important to try things such as forum, platform, dropbox, ad-hoc analysis etc. A great number may not work but if we keep the best ones and make a process with them, we can hopefully implement a good innovation finding process.

Perhaps, the last word could be a quotation from Woody Allen, which said: *“If you’re not failing every now and again, it’s a sign you’re not doing anything very innovative”*

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Conclusion (Français)

En premier lieu, un résumé de ce qui a été fait s'avère nécessaire:

- Un processus entier a été imaginé et mis en place
- Les recherches actives ont été préférées aux recherches passives
- Des parties du processus ont été éliminées car il n'y avait pas assez de ressources pour les faire fonctionner
- La partie analyse doit être consolidée
- 6 opportunités ont été finalement présentées après le processus de sélection. Ces innovations semblent pertinentes pour une compagnie dermatologique
- Trois analyses ad-hoc ont été réalisées pour trois différents départements, ceci n'a été possible que grâce au réseau établi pendant le stage

Ceci étant dit, plusieurs recommandations peuvent être mises en avant. La plus importante étant que des allocations de ressources sont nécessaires. Le personnel et les matériels sont indispensables pour établir ce genre de processus.

Concernant le personnel, il est important d'avoir un coordinateur pour faire fonctionner l'ensemble. En effet, un coordinateur est le lien entre les personnes. De plus, il peut jouer un rôle d'administrateur du site. A partir du moment où une personne est dédiée à l'innovation et que les collaborateurs sont au courant de ça, il devient plus facile pour n'importe qui d'aller lui adresser une demande concernant l'innovation. De plus le coordinateur peut rediriger la question à quelqu'un de spécialisé. Le coordinateur est une partie cruciale du réseau. A propos du matériel, la plateforme créée avec SharePoint présente beaucoup de limites. Si nous voulons que le processus soit fait sur mesure à la compagnie, il est important de pouvoir faire ce que l'on veut comme fonctionnalités, qui plus est, il faut que le site puisse évoluer en même temps que le processus. Ainsi, une page Internet est nécessaire. A côté de ça, si nous voulons faire de bonnes sessions de travaux (Workshop), du matériel peut être requis également ; le but étant de stimuler la créativité des gens. Dans tous les cas, le besoin de personnel est prioritaire à celui de matériel.

Une fois les ressources obtenues, il est crucial d'établir un réseau durable au sein de la compagnie. Une faiblesse d'un système de R&D classique est le manque de communication au sein et à l'extérieur de la compagnie.

Ainsi la mission principale d'un coordinateur serait de créer un réseau. Partant de ces principes, les collaborateurs auront une efficacité dans les échanges ainsi les projets avanceront plus vite.

A propos des technologies disponibles, nous savons que nous pouvons approximativement faire tout ce que nous voulons. Pour preuve, il est possible de surveiller toutes les routes d'administration, avec des patches, des pilules connectées, des nanorobots et autres. Le plus important est de déterminer ce que nous voulons faire, vers où la compagnie veut s'orienter. La vraie question n'étant pas « Comment fait-on ? » mais plutôt « Que voulons-nous faire ? ».

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Comme ça a déjà été exposé précédemment, tout changement va à l'encontre des engagements préétablis. Ainsi il est crucial d'identifier ces engagements et puis essayer d'être innovant tout en les considérant. De plus, il y a un grand besoin ; celui de l'engagement de la part du management sur des stratégies d'innovation. Sans quoi, rien n'avancera vraiment. Les personnes peuvent être divisées en plusieurs catégories (Innovateur, adopteur précoce, majorité précoce, majorité tardive et retardataires). Ainsi pas tout le monde n'adhère en même temps de manière naturelle à une nouvelle stratégie. C'est pourquoi les managers doivent prendre le taureau par les cornes et montrer les bénéfices d'une stratégie à son équipe. Le processus d'innovation a besoin d'être accepté par l'ensemble de la compagnie car c'est un état d'esprit et ce genre de processus s'appuie sur chacune des personnes présentes. Ceci est un point essentiel. En outre, au sein d'une grande compagnie qui existe depuis des décennies, le challenge est d'autant plus grand que dans des petites compagnies car le nombre de collaborateur à convaincre est encore plus important.

Pour conclure le sujet, être proactive est essentiel. Ainsi chercher une innovation sans but réelle est peut être inutile. Au contraire, quand une thématique est donnée (Ex, les anticorps bispécifiques), la recherche de l'innovation prends un sens mais pas seulement. Pour avoir la possibilité d'innover et de proposer la bonne solution, chercher une innovation n'est peut-être pas ce qu'il y a de mieux. Au lieu de cela, être innovant au sein de la compagnie en utilisant différentes méthodologies (ex, plateforme d'open innovation, workshop, veille collaborative), peut-être plus pertinent. Dans tous les cas, il est important d'essayer que ce soit un forum, une plateforme, une boite à question, des analyses ad-hoc... Un grand nombre peut ne pas marcher mais si on arrive à sélectionner les meilleures et en faire un processus avec, nous pouvons espérer avec quelque chose de robuste pour trouver de l'innovation.

Ainsi, le mot de la fin pourrait être une citation de Woody Allen : « Si vous n'échouez pas de temps à autres, c'est un signe que vous ne faites rien de très innovant »

VU ET PERMIS D'IMPRIMER

Grenoble, le : 13/11/2015

LE DOYEN et LE PRESIDENT DE LA THESE



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Annex

1. Table gathering Newsletter:

Name	Field	Interest for the mission	Unsubscribed before the end of the internship
Physorg	Generalist information	+++++	No
Science Daily	Biotechnology	++	No
Packaging news	Packaging	++	No
Medical news today	Generalist healthcare	+++	No
Labiotech.eu	Biotechnology	+	No
FierceBiotech	Biotechnology	+	No
FiercePharma	Generalist	-	Yes
FierceVaccine	Vaccinology	-	Yes
Mintel	Self-Medication	+/-	Yes
Gene Therapy Net	Gene Therapy	+	No
Cell Therapy News	Cell Therapy	++	No
In Pharma Technology	Generalist	-	Yes
Outsourcing Pharma	Outsourcing	-	Yes

2. Live form for submitting innovative ideas:

Name *

Surname *

Department *

Practice Area *

Pharmaceuticals
 Medical Devices and Diagnosis
 Consumer
 Cross sector
 Other
 Spécifiez votre valeur :

GBU *

Rx
 Self Medication
 A&C

Disease / Skin condition *

Spécifiez votre valeur :

Description *

Application *

Link

Entrez l'adresse Web : (Cliquez ici pour effectuer un t
http://
Entrez la description :
Add an URL...

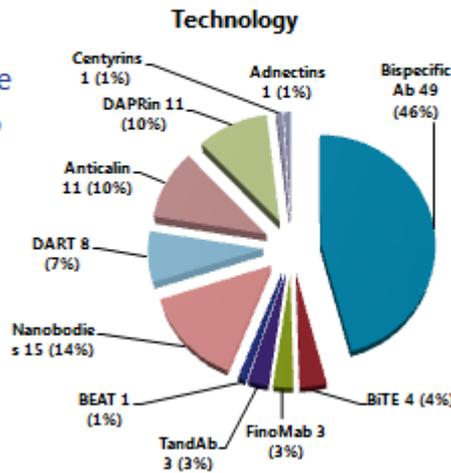
Other information?

3. Landscape bispecific antibodies (extract)

Bi-specific antibodies – Technology identified (2/2)

Nanobodies and smaller molecule are easier to produce and characterize, and can also bind sites not reachable by classical Ab

Alternative routes of administration, other than injectable, are under investigation

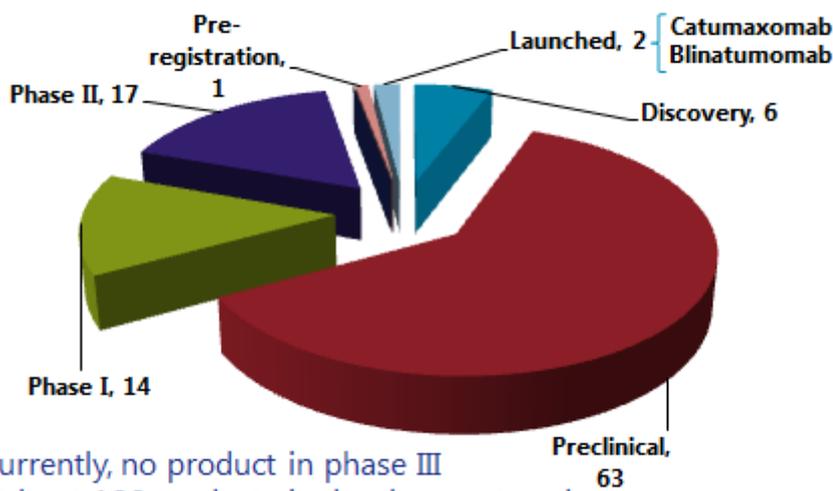


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Bi-specific antibodies in development



- Currently, no product in phase III
- At least 100 products in development and two marketed

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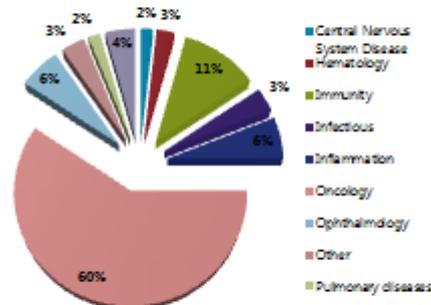
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Bi-specific antibodies – Indications in dermatology

- Among the different targets, four products are under development for dermatological indications

- Covagen and J&J for Psoriasis
- Immunocore and Eli Lilly for metastatic cutaneous melanoma
- Oncobiologics for Melanoma
- Sutro Biopharma and Celgene for Melanoma



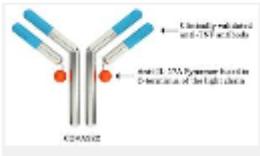
- Among direct Galderma's competitors, Allergan is working with Molecular Partners (on DARPin technology) and Pieris (on Anticalin technology) in ophthalmology

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COVA-322 (IL-17A and TNFa) Covagen and J&J

Phase II		
Drug Description	COVA-322 is an interleukin 17A neutralizing Fynomere, which has been fused to a fully human anti-TNFα antibody, under development for the treatment of Crohn's disease, psoriatic arthritis, psoriasis, rheumatoid arthritis and uveitis	
Phase 2	Randomized, double-blind, placebo-controlled, sequential, ascending single-dose, parallel group study to evaluate safety, tolerability, biological activity, and systemic exposure of COVA322 in 39 patients with stable chronic moderate-to-severe plaque psoriasis. Patients will receive ascending single-doses of COVA322 or placebo as a constant-rate i.v. infusion, followed by 12 weeks of evaluation (Identifier: NCT02243787)	
Preclinical	In in vitro, COVA-301 neutralized both IL-17A and TNFα with an apparent IC50 value of 30pM. It stayed monomeric and showed no signs of aggregation even after 4mth of storage at +4°C, -20°C or -80°C in PBS or after repeated freeze-thaw cycles. It was found to be stable after 5d of incubation in human serum at +37°C. It bound with human neonatal Fc receptor (FcRn) with the same affinity as the unmodified anti-TNFα antibody	
Estimation for Registration & Launch	Estimated primary completion date is November 2015 for Phase II. Submission could be expected in 2021. Best estimation for launch is 2022	
Covagen / J&J	This company located in Switzerland, was established in 2007. It is developing next-generation protein drugs for the treatment of diseases by using its Fynomertechnology. It was acquired by Johnson and Johnson in August 2014. The opportunity was identified and facilitated through the Johnson & Johnson Innovation Center in London.	

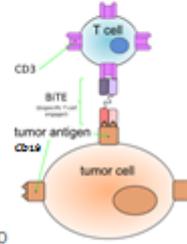
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Blinatumomab (Amgen Inc)

- Launched in EU as a treatment of acute lymphocytic leukemia as an orphan drug
 - Since little information exists through publication about its therapeutic benefit and adverse effect, it's not possible to conclude on advantage compared to conventional treatments
 - Clinical trial results:
 - 32% of patient had a complete remission after 2 cycles o median duration of the response was 6,7 month
 - 31% had a complete remission with or without complete hematologic recovery, but with reduction in minimal residual disease less than 10^{-4}
 - About the risks:
 - In patients receiving BLINCYTO in clinical trials, neurological toxicities have occurred in approximately 50% of patients
 - There is an high risk of Cytokine Release Syndrome



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Ablynx



Belgian Biopharmaceutical company engaged in the development of nanobodies: Protein based on single-domain antibody fragment

Competitive advantage due to its unique structure:

- Targeting different paths at once
- Small size: Reach epitopes usually hidden
- Alternative delivery route (e.g. inhalation, oral-to-topical)
- Customized half-life extension
- Conjugating several nanobodies together
- Ab drug conjugate (ADC) technology
- Easy manufacturing with increased yield (up mAb)



Weakness: Short half life due to small size

40 products under development, 6 at a clinical stage

Important collaborations with big pharma (e.g., Boehringer Ingelheim, Merck & Co, Novartis, Genzyme, AbbVie, ...)

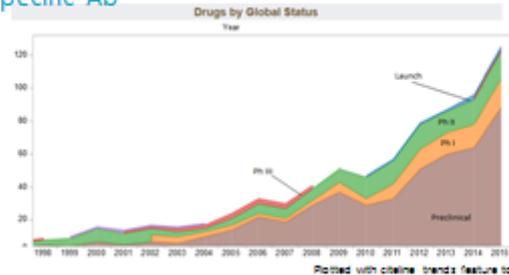
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Conclusion (1/2)

- High interest for bi-specific antibody technology
 - At least 40 companies with their proprietary technologies and platforms
 - At least 18 different approaches are identified to date
 - More than 100 products are in development, however only few products have advanced in late clinical development
 - A great number of big pharma companies have collaboration for developing Bi-specific Ab



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Conclusion (2/2)

- Two marketed product with limited efficacy; advantages compared to conventional treatments have to be demonstrated
 - Catumaxomab for treatment of malignant ascites EpCAM positive as second-line therapy
 - Blinatumomab for treatment of acute lymphocytic leukemia as an orphan drug
- Cancer is main indication, only four companies are working in dermatological indications (psoriasis and melanoma)
 - Covagen with J&J in psoriasis (Phase 2); Sutro Biopharma with Celgene and Oncobiologics in melanoma, both at preclinical stage; Immunocore in melanoma (Phase 2)

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4. Like or Throw committee, an example of proposed innovation

Innovation 3

Title: Internet Of Things (IoT) Sensor wristband

Description: Imagine a device that measure your skin moisture, sun exposure, even more, pollution of the air around you

Potential use: Using this connected object can help customer to know when and what kind of product he have to use according to his environment and skin. **No focus on dermatology yet except "sunscren's wristband"**

More news at:
[UV-sensor by Ultra Inc.](#)
[Environmental sensors](#)

Departments concerned:
- R&D
- Marketing
→ Self-Medication

Competition:
Focus on UV-sensor/exposition for skin but no other parameters
Ultra Inc. hold 50 patents

Like Throw

Add a comment...



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5. Snapshot of the Open Innovation platform made during the internship

Home page:



The screenshot shows the Galderma Open Innovation platform home page. The header includes the Galderma logo and navigation tabs for 'Open Innovation', 'About', 'Forum', 'Innovation', 'News', and 'Share your idea!'. A central banner reads 'Welcome to the Open Innovation platform' and asks 'First of all, during those last days, did you have an innovative idea? Share your idea here'. Below this is a 'REPORT' section with a cartoon character and the text 'Here you can find the report of the first Workshop (May 2015)'. The main content area features three columns: 'Forum' with a brain icon, 'Innovation' with a lightbulb icon and the text 'Let's have a look to last spotted innovations!', and 'Last news' with a 'NEWS' icon. At the bottom, a process flow diagram illustrates the innovation cycle: 'Problem' leads to 'Convert into innovation challenge', which leads to 'Challenge colleagues to suggest creative solutions'. This is followed by 'Collaborative idea generation', 'Combine & evaluate ideas', 'Develop ideas', and 'Implement most promising ideas', which leads to 'PROFIT!'. A small text box at the bottom of the diagram states: 'Corporate innovation = implementation of creative ideas in order to generate value, usually through reduced process costs, increased income or both.'

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About:

Implementation of a process of research of innovation within Galderma:

Working flow

The diagram illustrates a three-stage innovation process:

- I Innovation:** A green box labeled 'Spot innovation' leads to a green box labeled 'Archive'.
- II LoT (Like or Throw Committee):** A blue box labeled 'LoT (Like or Throw Committee)' receives input from the 'Archive' and outputs to 'Client 1', 'Client 2', and 'Client 3'.
- III Feedback:** A red box labeled 'Feedback' contains 'Follow innovation information' and 'News or Archive of CI activities'. Arrows show a cycle from 'Follow innovation information' to 'Feedback' and back to 'LoT'. 'News or Archive of CI activities' also feeds into the 'Feedback' loop.

Additional text on the page includes:

- Have a look at those presentations:**
 - Innovation process, by Jerome Topsent, April 2015
 - How to spot, analyze and follow innovation? by Jerome Topsent, March 2015
- Review and Webinar about Innovation in dermatology:**
 - Innovation in cosmetic (FRENCH), article from La Recherche n°499, Cosmetic Valley, Mai 2015
 - Innovation in packaging, by Jerome Topsent, April 2015
 - Self Medication and innovation, by Jerome Topsent, March 2015
 - The Internet of Thing Healthcare, by Dolcera, March 2015
 - Wearable Device Space, by Dolcera, December 2014

Forum:

Welcome to our forum!

We welcome your comments about ongoing subject and if you want to submit a new topic, go ahead!

Objet	Créé par	Réponses	Dernière mise à jour
Alternative to biopsy	TOPSENT Jerome	2	07/07/2015 10:50
WORKSHOP - May 2015	TOPSENT Jerome	1	30/06/2015 15:10
Pathological model of reconstructed skin	TOPSENT Jerome	2	28/05/2015 11:08
Adding a biological activity to a filler	TOPSENT Jerome	2	27/05/2015 14:18
The Internet Of Thing and Wearable Devices	TOPSENT Jerome	0	12/05/2015 09:47
Skin permeation	TOPSENT Jerome	0	11/05/2015 16:43

Innovation:

Artificial electronic skin

Artificial electronic skin is a wearable device. Through several sensors, it can monitor several biological parameters. It may also mimic skin functions for temporary prostheses.

Characterization: Technology is able to describe, it will be full of interest for you to watch the following video and the article [Supporting data for continuous non-invasive glucose monitoring.pdf](#) to understand the subject.

Competitive land scape and patent: Please see all trademarks but some big companies such as U-Dreal are working with these players for clinical trial's monitoring.

Research on Patent Implications: Research: TITEL-ABB-CLAIMS (1 + a skin -1) OR TITEL-ABB-CLAIMS (artificial electronic skin) OR TITEL-ABB-CLAIMS (artificial skin)
 ABB-CLAIMS (artificial skin)
 282 patents results, registered by family only 157. Work with the family:

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News:

GALDERMA News • Page d'accueil

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Calendrier
Tâches
Propriétés

Discussions
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Corbeille
Tout le contenu du site

July 10th, 2015: Scientists hack common bacteria in human intestines:



Therefore, scientists expect control guts and make it being able to respond to different sensors. The eventual goal would be able to engineer microbes that can alter gene expression based on signals within the intestines.
Read more at: <http://phys.org/news/2015-07-scientists-hack-common-bacteria-human.html#jcp>

Take the time to watch this video, Science can change the world, a message of hope



Source: <http://www.sciencecanchangetheworld.org/>

July 7th, 2015: Once again, skin shows new properties and advantages for many treatments:

RSS feed:

Scientific Information

Medical News TODAY

Dermatology News From Medical News Today

Lingering lymphocytes lash out against Leishmania
EC licenses MSD's immunotherapy KEYTRUDA (pembrolizumab) for the treatment of advanced melanoma
National Psoriasis Foundation launches patient-centered research platform Citizen Psoriasis connects patients, researchers to drive future research
FDA approve new daily pill for common skin cancer
NICE recommends innovative psoriasis treatment secukinumab, with three month window for NHS implementation

LABIOTECH.eu
The European Biotech News Website

LaBioTech

GenRight raises €33M to treat young adult blindness
Effective Antibody from a Patient recovering from Middle East Respiratory Syndrome
We met Antoine Hubert, CEO of Ynsect and awarded Innovator Under 35 by the MIT
Struggling AstraZeneca sells Rare Disease drug to Genzyme-Sandoz for €300M
Allergan Continues Its Serial Acquisitions to be a Giant Drugmaker

Dropbox:

Share your ideas
Innovation comes from everywhere, and for sure, today you feel innovative!



Do you have an idea or a probrtunity*? Share through our [submission form](#) or [send an email](#)
In every case you will receive a feedback, thank you for your involvement!

*Probrtunity is an all-inclusive word to describe something you want to improve or change for the better.

↓

Name *	<input type="text"/>
Surname *	<input type="text"/>
Department *	<input type="text"/>
Practice Area *	<input type="radio"/> Pharmaceuticals <input type="radio"/> Medical Devices and Diagnosis <input type="radio"/> Consumer <input type="radio"/> Cross sector <input type="radio"/> Other <input checked="" type="radio"/> Spécifiez votre valeur : <input type="text"/>
GBU *	<input type="checkbox"/> Rx <input type="checkbox"/> Self Medication <input type="checkbox"/> A&C
Disease / Skin condition *	<input checked="" type="radio"/> <input type="text"/> <input type="radio"/> Spécifiez votre valeur : <input type="text"/>
Description *	<input type="text"/>
Application *	<input type="text"/>
Link	Entrez l'adresse Web : (Cliquez ici pour effectuer un test) <input type="text"/> http:// Entrez la description : <input type="text"/> Add an URL...
Other information?	<input type="text"/>