Personalised Medicine in **France** and **Europe**: **a major health economic challenge**

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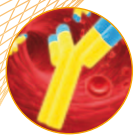
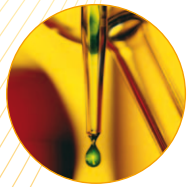




PROGRAM

Conference at the Palais du Luxembourg – Paris - organised by **EPEMED**

Tuesday 12 October 2010

"Personalised Medicine in France and in Europe: a major health economics challenge for the next decades"

Under the sponsorship of **Mr Senator Philippe Adnot**

9:00 am | Welcome

- **Mr Senator Philippe Adnot,** Chairman of the county council of Aube (in Champagne), member of the Finance Committee
- **Mr Alain Huriez,** MD, Chairman EPEMED, CEO TcLand Expression

9:10 am | Introduction

- **Mr Claude Birraux,** Member of Congress, President of Office of Evaluation of Scientific and Technological Choices

9:20 am | Plenary Session

- The challenges of Personalised Medicine **– Mr Alain Huriez, MD**

9:40 am | 1st Round Table

Personalised medicine, biomarkers, definitions, major progresses expected, translational research in France and health care organisations as source of innovations.

Moderator: Pr Fabien Calvo, Deputy General Director, National Cancer Institute (INCa) and Director AVIESAN Alliance for Cancer

- **Pr Jean Paul Soulillou,** Professor of Immunology; Director of Centaure Network, Nantes
- **Pr Philippe Beaune,** Chief Department of Biology & Head of Clinical Chemistry European Hospital Georges Pompidou (HEGP) - AP/HP
- **Pr Jean Charles Pomerol,** Chairman UPMC, Paris 6
- **Pr Pierre Miossec,** Professor of Clinical Immunology, Immunogenomics and Inflammation Research Unit, Hospices Civils, Lyon

11:10 am | 2nd Round Table

Access to innovations in personalised medicine, regulatory, economic challenges in France.

Moderator: Mrs Cécile Tharaud, CEO, Inserm Transfert

- **Mrs Cécile Vaugelade,** Medical Devices evaluation, AFSSAPS agency
- **M. Vincent Fert,** Chief Executive Officer, IPSOGEN
- **Dr Nadine David,** Head of Drugs Office, Health Direction, French Ministry of Health

12:30 | Lunch

1:30 pm | 3rd Round Table

Personalised Medicine, experience in the USA, the major medical advances. Impact on cost-savings on the Healthcare System. The next steps.

Moderator: Mr Patrick Terry Founder of International Genetic Alliance, Personalized Medicine Coalition, Genomic Health

- **Mr Edward Abrahams,** President, Personalized Medicine Coalition (PMC)
- **Mr Pierre Cassigneul,** President & CEO, XDx
- **Mr Felix W Frueh, PhD,** Vice President R&D Personalized Medicine Medco Health Solutions, Inc.

3:00 pm | The role of industry players in France

- **Mrs Catherine Lassale,** Director Scientific and Medical Affairs, Leem ('Les Entreprises du Médicament')
- **Mr Christian Parry,** Vice President French IVD Industry Association (SFRL)
- **Mr André Choulika,** President France Biotech, CEO Cellectis

4:00 pm | Biomarkers and Theranostics: dream or reality? The vision from a leading *In Vitro* Diagnostic company

- **Mr Christian Bréchot,** MD, Vice President Medical and Scientific Affairs, Institut Mérieux

4:15 pm | Strategic opportunity for innovative patient care in France

- **Pr Philippe Amouyel,** CEO National Foundation for Alzheimer's Disease, General Manager Institut Pasteur of Lille

4:30 pm | Conclusions and wrap-up

- **Mr Member of Congress Guy Lefrand,** MD, Member of Social Affairs Commission at the French Congress
- **Mr Alain Huriez,** MD, Chairman EPEMED

Facilitator: Mr Fabrice Papillon, Scientific journalist

PROGRAM

Conférence au Palais du Luxembourg organisée par **EPEMED**

Mardi 12 Octobre 2010

“ La Médecine Personnalisée en France et en Europe : un enjeu majeur de santé et de finances publiques ”

sous le parrainage de **Monsieur le Sénateur Philippe Adnot**

9h00 | Accueil :

- **M. le Sénateur Philippe Adnot,** Sénateur et Président du Conseil général de l'Aube, Membre de la Commission des Finances, Rapporteur des crédits de l'Enseignement Supérieur et de la Recherche
- **Dr Alain Huriez,** Président EPEMED, Directeur Général TcLand Expression

9h10 | Introduction

- **M. le Député Claude Birraux** Député de Haute-Savoie, Président de l'Office Parlementaire d'Evaluation des Choix Scientifiques et Technologiques

9h20 | Session Plénière

- Les enjeux de la médecine personnalisée - **Dr Alain Huriez**

9h40 | 1ère Table Ronde

La médecine personnalisée, les biomarqueurs, explications, définitions ; les grands progrès attendus; la recherche translationnelle en France et l'organisation des soins comme sources d'innovations

Modérateur : Pr Fabien Calvo, Directeur Général Adjoint de l'Institut National du Cancer (INCa), Directeur de l'Institut Cancer de l'AVIESAN

- **Pr Jean Paul Soulillou,** Professeur d'Immunologie, Directeur du réseau Centaure, Nantes
- **Pr Philippe Beaune,** Chef du Pôle Biologie et Chef du Service Biochimie à l'Hôpital Européen Georges Pompidou (HEGP) - AP/HP
- **Pr Jean Charles Pomerol,** Président UPMC, Paris 6
- **Pr Pierre Miossec,** Professeur d'Immunologie Clinique, Unité Immunogénomique et Inflammation, Hospices Civils de Lyon

11h10 | 2e Table Ronde

Accès aux innovations de médecine personnalisée, les enjeux réglementaires, sociétaux, économiques en France.

Modérateur : Mme Cécile Tharaud, Présidente du Directoire, Inserm Transfert

- **Mme Cécile Vaugelade,** Evaluation des Dispositifs Médicaux, AFSSAPS
- **M. Vincent Fert,** Directeur Général, IPSOGEN
- **Dr Nadine David,** Chef de bureau du Médicament, DGS, Ministère de la Santé

12:30 | Déjeuner

13h30 | 3e Table Ronde

L'expérience américaine de la médecine personnalisée ; les premiers grands progrès médicaux constatés ; l'impact sur l'optimisation des dépenses de santé ; les évolutions possibles.

Modérateur : M. Patrick Terry Fondateur International Genetic Alliance, Personalized Medicine Coalition, Genomic Health

- **M. Edward Abrahams,** Président, Personalized Medicine Coalition
- **M. Pierre Cassigneul,** Président, société XDx
- **M. Felix W Frueh, PhD,** Vice Président R&D Personalized Medicine Medco Health Solutions, Inc.

15h00 | Le rôle des industriels en France

- **Mme Catherine Lassale,** Directeur affaires scientifiques et médicales Leem (Les Entreprises du Médicament)
- **M. Christian Parry,** Vice Président du SFRL
- **M. André Choulika,** Président de France Biotech, Directeur Général Cellectis

16h00 | Biomarqueurs et Théranostique : rêve ou réalité ? Vision d'un groupe de diagnostic, leader mondial

- **Dr Christian Bréchot,** Vice Président Affaires Médicales et Scientifiques, Institut Mérieux

16h15 | Opportunité stratégique pour une offre innovante des soins aux patients en France

- **Pr Philippe Amouyel,** Directeur Général de La Fondation Nationale de Coopération Scientifique Maladie d'Alzheimer et Maladies Apparentées, Directeur Général de l'Institut Pasteur de Lille

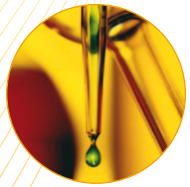
16h30 | Conclusions et fin

- **M. le Député et Dr Guy Lefrand,** Membre de la Commission des Affaires Sociales à l'Assemblée Nationale
- **M. Alain Huriez,** Président EPEMED

Facilitateur: M. Fabrice Papillon, Journaliste Scientifique

EPEMED
CONFERENCE REPORT

EXECUTIVE SUMMARY (English)



Summary of EPEMED's Personalised Medicine Conference, Paris, 12 October 2010

EPEMED, the European Personalised Medicine Association, a not-for-profit organisation bringing together global forces in personalised medicine, organised its first conference in collaboration with the French Senate in Paris on 12 October 2010. The conference was entitled "Personalised Medicine in France and Europe: a major health economic challenge". The purpose of the meeting was to inform and educate policy makers, industrial players and other interested parties on the broad challenges associated with access to personalised medicine in Europe, with a particular emphasis on France. It was hosted by French Senator Philippe Adnot, member of the Finance Committee, who introduced the conference together with the French Member of Congress Claude Birraux. The conference attracted a diverse group of attendees from Europe and the United States. The meeting was structured as a plenary session presented by EPEMED's chairman Dr Alain Huriez, followed by a series of 3 round tables, together with several presentations followed by a discussion of the role of French industry.

Dr A. Huriez

Senator P. Adnot

The first round table was formed by five senior French academic scientists and discussed the concept of personalised medicine and in particular the innovations coming from translational research in the public sector. The session, which was chaired by Professor Fabien Calvo, Director General of INCa (Institut National du Cancer), highlighted INCa's 28-center PM testing network, whereby INCa funds emerging tests while they progress towards standard of care, thereby facilitating early access. This network currently offers or will soon offer, EGFR, K-Ras, B-Raf, EML4-ALK, and HER-2 testing.

The second round table, building on Professor Calvo's theme, was focused on market access, including regulatory and economic challenges. Chaired by Cecile Tharaud of Inserm Transfer, the panel included Cecile Vaugelade (head of Evaluation at AFSSAPS), Dr. Nadine David (Head of Drugs Office, French Ministry of Health), Vincent Fert (CEO of Ipsogen). This session included a lively discussion of the challenges associated with the commercial development and clinical laboratory provision of complex tests

and of the law of Ballereau which limits the sites at which molecular diagnostic tests may be carried out, including the role of corporate sponsors. In particular, the French prohibition of the kind of commercially led activity common in the US and other markets was seen as a force driving French innovation overseas.

The third round table was focused on the US experience regarding personalised medicine. Chaired by Patrick Terry, co-founder of Genomic Health, the panel included Ed Abrahams (President of the Personalised Medicine Coalition), Felix Frueh (Vice-President of Personalised Medicine, Medco), and Pierre Cassigneul (CEO of XDx). The panel highlighted the more advanced status of PM in the US versus Europe. Felix Frueh presented Medco's US data illustrating the reduction in hospitalizations (around 30%) following the introduction of CYP2C9 and VKORC1 genotyping before prescribing warfarin in a six month study. Medco's personalised medicine program has already demonstrated improved patient outcomes by implementing diagnostic testing prior to dispensing certain drugs. The company, which can employ such approaches effectively as its data are nationally wired and real-time, has already made significant cost-savings following the introduction of its personalised medicine program. Pierre Cassigneul noted that the XDx AlloMap test used to predict organ transplant rejection is reimbursed by various US payors but, because of Europe's complexity, the test is currently not being marketed in Europe. However, an advantage for the introduction of personalised medicines in Europe was noted by Patrick Terry who stated that the European single payor systems presented an opportunity for a more cohesive approach to the market than the segmented US system.

The next session of the conference discussed the French industry perspective. Christian Parry (Vice-President, SFRL, the French Syndicate of In Vitro Diagnostic Industry) highlighted the size of the European in vitro diagnostic market with around 10 billion in annual sales (in 2008; more than a third of global sales) with Germany, France and Italy representing the largest markets. Although there are a number of companion diagnostic test on the French market, Christian Parry stressed the hindrance of new companion diagnostic development through increasing regulations and quality control processes. Also reimbursement frequently limits new test availability and the initial costs are currently often covered by the industry as a necessary interim step. Mr. Parry suggests that faster market access to novel personalised medicine diagnostic tests may be achieved by 1) collaborations between various parties (In Vitro Diagnostic industry, pharmaceutical and biotechnology companies and academic research groups), 2) adherence to in vitro diagnostic standards and development processes and 3) improvement of reimbursement procedures. In his talk on diagnostic test development in France, Andre Choulika (President of France Biotech), highlighted the fact that there is an increased delay in diagnostic development time in 2009 compared to 2008, which can be explained by an increase in financial and funding issues. Christian Brechot (Vice-President of Medical and Scientific Affairs, Institut Merieux) noted the considerable challenges and expenses associated with development of novel diagnostics,

spanning the need to demonstrate analytical and clinical validity, clinical utility and health economic impact. He did, however, stress the strategic and economical benefits for both pharmaceutical and biotechnology firms to collaborate with diagnostic companies to develop personalised medicines and companion diagnostic tests.

The conference was completed with an excellent overview by Professor Phillippe Amouyel (CEO, National Foundation for Alzheimer's Disease, General Director of Institut Pasteur, Lille) of the latest clinical evidence of how personalised medicine approaches can have great impact on patient outcomes with particular emphasis on Alzheimer's disease and myocardial infarction. Philippe Amouyel also presented the recent plans of Neximed, a university hospital institute, which aims to become a premier research site uncovering novel approaches in personalised medicine.

In conclusion, EPEMED's first conference highlighted the recent advances made in personalised medicine but also discussed the difficulties in making personalised treatments available for patients in Europe. The not-for-profit organization is preparing proceedings of the conference as a white paper which may be downloaded from its website (**www.epemed.org**) early 2011. EPEMED is planning further events, including another conference in 2011.

Christian Parry (SFRL)

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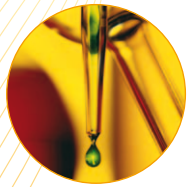
CONFERENCE REPORT

FULL PROCEEDINGS (English)



Personalized Medicine in France and Europe: A Major Development in Health and Health Care Costs

French Senator Philippe Adnot, Chairman of the county council of Aube and member of the Finance Committee kicked off the conference by contextualizing personalized medicine in the larger realm of the economy, pointing out that tailoring medical treatment to a patient with biomarkers not only means a more efficacious treatment but also a more economic delivery of treatment. Within the context of the spiraling national deficit, more economic delivery of services is an urgent priority.

Senator Adnot was joined by Member of Congress Claude Birraux Deputy of Haute Savoie and President of Office of Evaluation of Scientific and Technological Choices, in introducing the meeting, as well as by Alain Huriez, President of EPEMED, and Chief Executive Officer of TcLand Expression. The meeting was moderated by science journalist Fabrice Papillon.

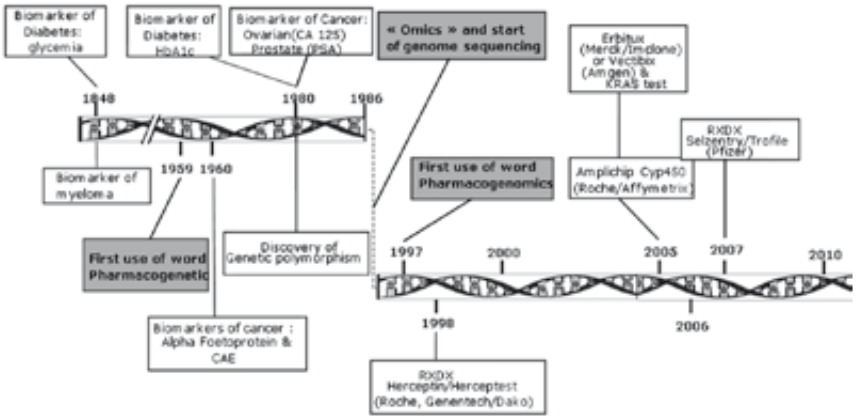
Alain Huriez pointed out that the conference had brought together representatives from a wide range of fields: scientific, medical, economic, institutional, industrial and journalistic. This wide range, he explained, *"is very representative of the multidisciplinarity of personalized medicine and its medical and economic impact."*

Personalized medicine holds out the promise of a more *"just distribution of financial resources for the politics of health care as a whole,"* in the words of Claude Birraux, but he cautioned that there are challenges to be overcome. It is not only technology that will drive the full expansion of personalized medicine – the education of practitioners needs to keep pace with technological advances.

Plenary opening session was presented by Alain Huriez who presented the definition of Personalized Medicine. The last century has seen a revolution in modern medicine with the discovery of many new treatments for common diseases. However, inter-individual variation means that response to treatment varies widely, which makes the blockbuster model of the Pharmaceutical industry (i.e. one drug suits all) highly costly, both from a patient health and economic point of view.

With the advent of the advances in technology for the "omics" approaches (genomics, proteomics, metabolomics etc.), the blockbuster model is gradually being sidelined for a model of so-called personalized medicine (PM). PM can be considered as a tailored approach to patient treatment based on the molecular analysis of genes, proteins and metabolites. PM is therefore causing a paradigm shift from a treatment-centred health system to a comprehensive patient-centred disease management approach.

Biomarkers and PM are included in medical practices since the 19th century but their development has accelerated in the last decade.



Furthermore Medical Genomics has still huge potentials for disruptive changes as described in the graph below, this should accelerate the progresses of Personalized Medicine in the forthcoming decades.

Time Period	Genomes	Turn around time	FTEs	Cost per genome
1990-2003	1. NIH reference 2. Celera reference	~5 years	~5,000	~2-3 billion USD
2003-2009	10 additional (next slide)	~6 months	Dozens	300,000 ➜ 38,000 USD
2010-2014	10^3-10^4	2-4 weeks	3-4*	3,800/19,500 ➜ 1,000 USD
2015-2020	Millions	15 minutes	<<1	100-250 USD

As a result, the next medicinal practices will move toward rationalised therapies:

Alain Huriez concluded the plenary session by reminding that France has great potentials to become a leading and pioneering country in Europe in the field of Personalized Medicine (Science, Healthcare systems, mathematics and Statistics…) but has also hurdles to overcome such as the organization of its local medical laboratory network, a better pharmacoeconomics classification of theranostics and an easier market access of molecular diagnostic technologies under validation.

1st Round Table:

Personalized Medicine, Biomarkers, Definitions

Individual Patients, Individual Cancers

Fabio Calvo
Director General of INCa (Institut National du Cancer)

Cancer embodies the challenges confronting personalized medicine and, at the same time, the advantages of personalized medical treatment. Breast cancer was one of the very first diseases to show measurable and reproducible results that proved targeting the specific type of breast cancer affecting a patient provides a more effective treatment than delivering to all patients the one treatment that has shown some overall positive results in the general population of breast cancer patients.

"Each human differs from every other one in a variety of ways, ranging from the basic genetic constitution of one individual to the various external factors that affect the development of a given population: people who breathe the same air, eat foods from the same areas, drink water from one common source. These epigenetic factors influence each person's genetic constitution over time and can provoke mutations, rearrangements, and variations in the number of genes, and, in some cases, the creation of specific tumors and their progression."

The challenge of cancer research, then, is to identify the genome of the different tumors and the variations on this genome in different individuals in order to better understand the specific cancer and thus better predict an individual's response to treatment. That is the goal of personalized medicine: to tailor treatment to the specific cancer in one particular individual.

Personalized medicine in France is evolving under the aegis of a presidential plan: the Cancer 2009-2013 Plan. This plan guarantees equal access for everyone to regional sites focused on the molecular genetics of cancer: laboratories, university research centers, hospitals, cancer research centers. At these sites patients have access to innovative molecular tests to target their specific cancer.

In the case of colon cancer and lung cancer this system has delivered some remarkable results.

- Implementation of the KRAS test for colorectal cancer allows doctors to distinguish between patients who will respond to an effective but toxic treatment from those who will not respond. The KRAS test is given free of charge to patients in a given region. As of 2009, about one year after testing began to be implemented, almost 20,000 KRAS tests had been administered, representing about half of all colon cancer patients in France.
- Research on the KRAS gene has also permitted the development of new tests that allow doctors to ascertain if a lung cancer patient will or will not respond to a specific therapy. While lung cancer has been a disease with few treatment options until recently, research into the mutations of the KRAS gene, the EGF gene, and translocations of the EML/ALK gene finally offers a way to predict reliably the responsiveness of a given patient's cancer to specific therapies.

In 2011 a new treatment for lung cancer, based on the EML/ALK translocation, will become available. This development illustrates how personalized medicine is driving the findings of genetic research out of the laboratory and into the hospitals where patients may experience if not remission, at least a reprieve from toxic treatment that has no chance of success in their case.

Personalizing Post-Transplant Care

Jean Paul Soulillou
Professor of Immunology and Director, Réseau Centaure, Nantes

In the case of transplant patients, personalized medicine may also serve to sort patients into different categories allowing for better, more efficient care.

Transplant patients require regular monitoring. For some patients this may involve a long, difficult trip to a regional center, waiting to be seen, and a day filled with anxiety about rejection. *"This means about 50 to 60 patients a day who travel 300 or 400 kilometers to see the doctor, and wait hours to have a needle injected, then stay until the results are in so as to avoid going home in a state of high anxiety."* The exam represents a cost to the health care system. Depending on the individual patient and the specific response to the transplant, however, some of these regular exams could be conducted remotely. With diagnostic biomarkers it should be possible to sort patients into those who do require regular in-person exams and those who can be assessed remotely because they have a lower risk of rejection. This would improve the quality of care for transplant patients and lessen the financial burden on the healthcare system.

In addition to regular monitoring, transplant patients require immunosuppressant drugs immediately after surgery and for some time afterward. These drugs have side effects that can adversely impact quality of life and can even be life-threatening. In the case of certain transplants and for individual patients, reducing or even eliminating the immunosuppressant drugs can mean the end of these side effects. Some liver transplant patients do well after these drugs are phased out of their treatment – 10 years after the transplant, 65% of patients do well without the drugs they initially required to prevent rejection. For certain other transplants and other patients, it is not possible to ever reduce or eliminate immunosuppressant drugs. It is vital to distinguish with absolute acuity between these two categories of patients.

Reducing Toxic Side Effects through Genetic Testing

Pierre Miossec
Professor of Clinical Immunology, Immunogenicity and Inflammation Unit, Hospices Civils de Lyon

Progress in treating rheumatoid arthritis is accelerating: with the introduction of biotherapies ten years ago, we have passed from one single anti-TNF to three today and soon will have five. But 40% of all patients do not respond to the first anti-TNF administered, and targeting the molecules of the immune system with an anti-TNF exposes the patient to infections, including tuberculosis. In addition, each time an ineffective anti-TNF is administered it represents a cost to the healthcare system that is pure waste. In the case of patients with rheumatoid arthritis this cost can be about 5 to 10 thousand Euros a year. The quest, then, is for biomarkers that will allow doctors to identify which anti-TNF agent will produce a favorable response in a given individual without trial and error.

These molecules are proprietary and represent a substantive investment for a pharmaceutical company – having a drug erroneously labeled harmful after use on patients represents a substantive loss. The anti-TNF Remicade was at one point suspected of causing leukemia in a patient. More exact analysis using biomarkers, however, showed that the leukemia was present before the administration of the drug, saving Remicade for the doctor's arsenal against rheumatoid arthritis. *"For the medical industry, biomarkers can not only save lives but molecules."*

Pharmacogenetics and Public Health

Philippe Beaune
Department Head, Biochemistry, at the Georges Pompidou European Hospital (HEGP)

Dosage that takes into account the patient's weight, age, and condition is not as precise as dosage that takes into account the patient's DNA. Pharmacogenetics studies the influence of variations in the DNA sequence on patient response to medical treatment. Absent this type of precise data on exactly how a patient with a given DNA sequence will respond to a drug, a drug that helps one patient may actually harm another patient with the same disease.

At the present, however, imprecision in dosing generates a public health problem: iatrogenesis, i.e. adverse side effects that can be fatal. 600,000 patients take anti-coagulants, but these drugs are the number one cause of adverse side effects with 17,000 hospitalizations/year and 4,800 deaths/year. More deadly than automobile accidents!

Taking genetic factors into account, however, decreases the chances of adverse side effects by matching more closely the anticoagulant dose to the patient's DNA. Specifically genetic anomalies on two genes can increase by a factor of 12 the risk of excessive bleeding for patients on Warfarin. Identifying patients with these genetic anomalies greatly diminishes the risk of adverse or fatal side effects from Warfarin.

Similarly in the case of patients being treated for a cancerous tumor, taking into account both the patient's genome and that of the tumor allows doctors to target more precisely the tumor while decreasing the chances of adverse side effects. Tests that analyze the patient's genome and that of the tumor are not only available but are in some cases required by regulatory agencies.

These challenges aside, personalized medicine is creating a future where *"medical treatment will no longer be one-size-fits-all but rather tailor-made."*

Education and Information Technology

Jean-Charles Pomerol
President, Université Pierre et Marie Curie, Paris 6

The future where medical treatment is tailor-made will mean a world with fewer patients dying from adverse side effects and more patients receiving targeted treatment for better outcomes. In order to reach this point two challenges must be overcome: that of educating healthcare providers and of

developing information technology robust enough for the demands of a level of precision previously unimagined.

"A nurse in a hospital today gives an injection to a cancer patient, then moves on to the next cancer patient and gives the same dose of the same drug. With the advent of personalized medicine, this routine will become more complicated as each patient with the same disease at the same stage must receive a drug that is personalized to the patient and to the patient's cancer."

As drugs are personalized to individual patients, a tremendous amount of data is generated about the patient. This data needs to be managed electronically and delivered along a pipeline to more scientists and doctors than have previously been involved in the treatment of one patient. Managing a database of this complexity is in and of itself a challenge for information technology, but it generates a second challenge: that of the ethical issues that can arise as more information about a patient is shared with more people.

Discussion: Ethical Questions

Non-Responders

In the case of a patient in a coma, for whom there is no possible medical treatment, the choice to continue or discontinue life support is a matter of life or death. The present state of personalized medicine may not be as exact as it needs to be to allow physicians to remove life support from a coma patient based on a companion test indicating the patient will never respond to treatment. Fabien Calvo stated: *"Certainly it is important to assess the prognosis of coma patients, to know just how far one can go and go all-out, but on the other hand, one cannot go past the point of no return, give up on treatment at such-and-such a moment."*

There are less extreme cases, however, that raise ethical issues and these cases involve patients who are unlikely to respond to a drug that could treat their disease. Should a doctor tell a patient that she has no hope of responding to treatment because the biomarkers show she is a non-responder? Should the doctor tell the patient that although the biomarkers show she is a non-responder there is nonetheless one slim chance that she might respond?

At this point the question of cost is involved. Should economics be permitted to limit the administration of drugs to patients whose companion test indicates they will or will not respond? This could mean reducing the administration of certain drugs from 100% of all patients to the 25% whose test indicates they are responders.

There is a further layer of complexity to this ethical issue: adverse side effects. In some cases administering a drug to a patient to treat a disease causes debilitating even potentially lifethreatening side effects. Limiting the administration of a toxic drug to responders means that nonresponders will be spared the ill effects of a drug that is useless to them. This is true in the case of the KRAS test for the treatment of colorectal cancer.

In the case of an extraordinarily expensive drug, treating non-responders may not be feasible at all. For lung cancer patients, the presence of recently identified mutation of the EML-ALK gene indicates that an extraordinarily expensive drug can mitigate the progression of the disease. Only 5% of all lung cancer patients have this mutation. They need to be identified and treated, but there can be no question of treating the 95% of patients who do not have the mutation.

Similarly in the case of a drug that can cause an extraordinarily expensive side effect, it is worthwhile to identify the small percentage of patients who are susceptible. The auto-immune suppressant Azathioprine can provoke myelotoxicity in a very small percentage of patients. While the actual number of patients may be small, perhaps 3/1000, the cost of treating myelotoxicity is so great that it is cost-effective to run the tests necessary to identify those 3/1000 patients in order to avoid them developing this potential adverse side effect.

The bottom line in the ethical issue surrounding decision-making with patients whose companion test indicates they are non-responders is that as long as personalized medicine is not 100% accurate, patient involvement in decision-making will have to fill the void. One participant proposed: *"It is up to the patients to participate in the discussion knowing that the treatment will be administered during 10 to 18 months, with substantive side effects."* This may mean asking a patient to decide whether or not to opt for a treatment that has only a 3% chance of mitigating the progression of his or her disease. In the case of a treatment that has debilitating side effects the decision may be even more difficult.

There are cases, however, where the data is so unambiguous that the doctor may have to tell the patient: *"there is nothing we can do for you."* This happens in the case of advanced pancreatic cancer, for example. In this scenario, palliative care may do more for the patient than ineffectual treatment.

Involving patients in the decision-making process is complex. For patients with no background in medicine or science, the data may be impossible to assimilate, especially as it is emotionally charged for the patient. Additionally there are cultural factors that make for different expectations with regard to the medical decision-making process. American patients are more likely to expect to participate in the decision-making process than their European counterparts who expect the healthcare system to generate a decision for them.

Use and Storage of Patient Data

As personalized medicine evolves an almost infinite amount of data about the human genome and patient DNA is generated. Within this wealth of data, however, there are problems of reproducibility. The data about one type of tumor's response to a specific drug, for example, may vary from one laboratory to another. One company's version of a given biomarker may not be exactly the same as another company's. Evaluations of companion tests may not be reproducible, which introduces an element of error into an area of research aiming for an unimaginable degree of accuracy. Further scientific research is needed to bring personalized medicine to this degree of accuracy, but at the same time protocols need to be put in place to ensure that all laboratories use the same means to achieve the same, reproducible, results.

Data about the human genome and patient DNA is derived from molecular patient samples that are used to make decisions about treatment. These samples do not vanish after the treatment or even after the death of the patient. Clearly the stewardship of these samples raises complex ethical questions and has given rise to vastly different regulations in different countries.

In France, for example, a patient may give consent for their tumor to be subjected to genetic testing for the purpose of determining the best possible treatment. After the patient's death no further testing for research purposes may be performed on the tumor even though such research holds the promise of generating new and better treatment for other cancer patients. In other countries such research is legal. Christian Parry, Vice President of SFRL explained: *"There is no simple answer because there is a juridical abyss and when one tackles questions such as these it becomes even more complex! And let's not forget: we can treat patients and save lives."*

Just as using the genetic data gathered from patients who are deceased may prove a fruitful source of information for scientists looking for new drugs to treat the living, so a national databank of genetic information of all citizens could be of great use. With the storing of genetic information on everyone living in the country, however, the potential exists for misuse or abuse of the information.

It will be necessary, however, to develop regulations and protocols that will permit scientists to gather genetic data on specific populations as this information is essential to validate the tests and drugs that are central to the promise of personalized medicine

2nd Round Table:

Market Access: The Pace of Innovation and Regulation

The Untapped Market of Pharmacogenetics

Cécile Tharaud
President, Inserm Transfer

For all its infinite potential pharmacogenetics has not yet begun to be fully exploited. For example, of the 850 patents requested in France last year, 50 were for biomarkers. This number increases by 10% every year testifying to the steady rate of discovery taking place in laboratories. Yet there is a gulf between the biomarker's patent application and its spot on the pharmacy shelf: biomarkers represent only 5% of all licenses granted and are the basis of only 10% of start-up companies. Science is producing results in terms of biomarkers discovered but industry is slow to follow up with products. Concerns about regulation and reimbursement *"make companies balk at taking out a license, make future entrepreneurs hesitate to write a business plan."*

Bottlenecks on the Road from Laboratory to Hospital

Nadine David
Head of Drugs Office, French Ministry of Health

Regulation of drugs coming into the market is complex and involves delays and work-arounds. For some medications, the companion test comes into the market years after the drug itself – as in the case of the antiretroviral Selzentry. While the drug was on the market without the corresponding companion test, the company paid for development of the test by sending them to the US to be evaluated.

Once a drug is regulated, reimbursement for the drug must be structured. This is a complex matter. In the case of cancer, for example, the cost of personalized medicine is two to four times higher than that of conventional chemotherapy. Who will cover this cost? "The objective is to spend well rather than spend less." Sometimes when reimbursement protocol is pending, regional treatment centers in France will offer the new drug free of charge in the interim.

Regulating the Biomarker/Companion Test Package

Cécile Vaugelade
Head of Evaluation, French Health Products Safety Agency
(Agence française de sécurité des produits de santé - AFSSAPS)

Biological innovation has surged ahead of healthcare regulation creating a time lag between existing treatments and the regulation that is needed to make them available to patients. This is because personalized medicine has in effect created a new medical treatment: it's not one drug it's the package of a targeted therapy and a biomarker-based companion diagnostic that indicates whether or not targeting this molecule will reverse disease in a given patient. From the reimbursement regulator's perspective, this is a new animal. *"Companion tests simply cannot be reimbursed in the present system because the category doesn't exist!"*

The new molecules are being created at diverse sites that fall under different authorities: academic laboratories and laboratories owned by private companies. When a new molecule has been created that turns out to have medical applications, at what point in its development do healthcare regulations take over? These regulations aim to protect public health but have the effect of delaying the entry into the market of a new molecule with medical applications.

In an ideal world, a biomarker would be developed simultaneously with its companion test in a laboratory regulated by the healthcare system in such a way that both would enter the market at the same time after tests on both had been conducted to protect patients from adverse side effects or ineffective treatments. The present situation is infinitely more complex, with different rules in effect for different types of laboratories, for different types of drugs and treatments (with the distinction between these two terms at issue), and in different countries.

Regulatory Road Blocks

Vincert Fert
Chief Executive Officer, Ipsogen

The difference between American and French regulations has resulted in a significant degree of movement away from France, toward America. *"Today, the very great majority of monoclonal antibodies—a very expensive drug category that is used in cancer treatment—is supplied by American laboratories. Biomarkers must not go the way of these antibodies."*

While it is true that substantive regulation is needed to protect patients, substantive regulation also increases the cost of a drug for patients. Within personalized medicine, the regulation that is being developed around this field proceeds at an uneven pace. The regulation of companion diagnostics lags behind that of biomarkers. Although these are very different areas of discovery, the need for clarity in both cases is the same. And clarity is what the industry needs.

Discussion: Delays in Regulations, Delays in Patient Access

Pharmacogenetics has evolved from the science of medical biology, which carries at its core an ambiguity from the perspective of regulators: is it medicine (i.e. healthcare) or biology (i.e. science)? A further level of confusion arises with the entry of pharmacogenetic products into the market place, as we are seeing not only new drugs but new, previously unimagined, types of companies producing and offering these new drugs. Once again, healthcare regulation has fallen behind biological innovation. Laws designed to protect public health delay patient access to the new therapies. France's "Loi Ballereau," for example, dictates that in a 'biological medicine laboratory' 75% of the capital must be owned by pharmacists or medical biologists. These types of regulations put a damper on the growth and profitability of pharmacogenetics. To keep pace with science, a new definition of medical laboratory is needed and should exclude start-up companies developing molecular diagnostics to respect *"their status as young innovating enterprises, massively investing into R&D and exploiting proprietary or licensed patents,"* suggested Alain Huriez.

3rd Round Table:

The American Experience of Personalized Medicine

New Science, New Business

Patrick Terry
Co-Founder, Genomic Health

The American equivalent of EPEMED is the Personalized Medicine Coalition. While in France, regulations have hampered the development of a new business model for biological medicine, in America innovative start-ups have been created that show what this business model should be. The goal is to translate the generalizable discoveries from genomics to the marketplace for advanced diagnostics, but there are different business models for attaining this goal.

At Genomic Health the research focused on breast cancer, over the last two years their activities have extended to more disease areas, to the point where these represent about $400 million in venture capital financing.

Traditionally a biomarker was seen as a single entity, such as gene mutation, but in the United States and elsewhere, researchers are starting to look at multiparametric markers an even getting to the point where they are not relying on a single technology, but using many molecules at once.

Foundation Medicine in Cambridge, Massachusetts (founded by Patrick Terry) can generate 2.6 terabytes of data on an individual's genome. The business model here is embedding the diagnostic enterprise into the clinical setting – being a partner with specialty physicians.

Theranostics links the diagnostic reality of newly discovered subtypes or subcategories of a given disease with the medical therapy derived from this diagnostic reality. Validating this emerging medical therapy through clinical trials and cohort studies that answer thousands of questions about the disease molecule while simultaneously generating effective treatment introduces a new level of complexity into validation.

In genomics today, "information is driving science." A newly identified disease molecule can deliver different insights into disease at the molecular level, and some of them have inherent applications that can be generated from them. This explosion of data, however, generates a new challenge for medical biology: how are we going to interpret these massive amounts of complex data?

These scientific discoveries occur in a regulatory context that varies from healthcare system to healthcare system. Under American's employer-based healthcare system, cost has become the determining factor. Under France's single payer system, patient outcome is the determining factor. There are also *"a lot of questions that the regulatory agencies and funding agencies will need to deal with in this arena."*

Economic Advantages of Personalized Medicine

Edward Abrahams
President, Personalized Medicine Coalition

Genomics shows that different patients at the same stage of a given disease are in fact very different one from the other at the molecular level. It makes sense, then, that different treatments, personalized treatments, will produce better outcomes. And indeed, in the present state of medicine as it is, drugs that were created prior to the development of personalized medicine, are actually quite ineffectual: 50% of drugs don't work! Patients with hypertension or depression are treated on a trial and error basis: try one drug if that doesn't work try the next one. The cost of this trial and error method of prescribing drugs is astronomical.

In contrast, the development of new drugs that target leukemia molecules with greater precision has increased 5-year survival rates from 0 to 70%. Consider what might have happened with Vioxx if Merck had developed a companion diagnostic alongside the drug: patients who were at risk of adverse side effect would have been identified and would not have been given the drug.

The advantages and cost-savings of personalized medicine are evident, and yet the full implementation of personalized medicine is still impeded by physician resistance.
As Fabrice Papillon said in welcoming participants to the conference: *"personalized medicine is something that everyone has heard of without fully understanding precisely what it is."* This is even true to a degree among the medical community, where practitioners do not appreciate that personalized medicine means targeted therapies.

Benefits to Patients of Molecular Diagnostics

Pierre Cassigneul
CEO, XDx

For some patients targeted therapies can mean not just experiencing better outcomes but avoiding massively invasive procedures or extremely toxic side effects. The molecular diagnostic company, Xdx, is developing and evaluating companion diagnostics that can spare heart transplant patients the agony of regular heart biopsies and can help patients with lupus avoid a very toxic treatment when it is unnecessary.

Heart transplant patients undergo approximately 20 to 35 heart biopsies in the five years following the transplant. During a biopsy the surgeon cuts off a slice of tissue from the heart for testing: the results indicate if the patient is in danger of rejecting the heart. These biopsies cost about $1,800-$2,000. XDx has developed a blood test, AlloMap, that is designed to deliver the same information as a heart biopsy. From 2001 to 2005 a study of 630 patients was conducted comparing patients evaluated using heart biopsy and patients evaluated using AlloMap. The results showed that the blood test was as accurate as the heart biopsy – these results were published in the **New England Journal of Medicine** in April 2010.

XDx is also developing a companion diagnostic to help lupus patients. This is a disease that comes and goes in crises. When a patient is not about to experience a crisis there is no need for the treatment, which causes toxic side effects. The challenge is to predict when a crisis is imminent. The companion diagnostic under development is designed to do just that.

A Value Proposition for Payers: Personalized Medicine

Felix Frueh
Vice-President, Personalized Medicine Medco

Once a companion diagnostic has been developed, it needs to reach the patient. Medco is a pharmacy benefit management company that uses companion diagnostics and in so doing is reducing costs to the healthcare system. Medco manages the outpatient drug benefits of a wide range of insurers, filling about 300 million prescriptions annually.

Surveys have shown that both payers and physicians are all extremely interested in the benefits of pharmaceutical genomics. Payers put pharmaceutical genomics at number 2 in their list of what they think could help manage costs in the long run. 99% of physicians surveyed believe that genetics is important for drug therapy – yet 57% of them have never used the relevant technology because they have no information about it.

For patients, the benefit of pharmaceutical genomics can best be illustrated by looking at adverse side effects of Warfarin. An observational study conducted in collaboration with the Mayo Clinic looked at hospitalizations of patients on Warfarin due to a bleed or an embolism. Hospitalization is a useful measure in evaluating the cost of medical treatment because you can precisely calculate the price of treating a patient. The results showed a 30% reduction in hospitalizations of patients who are treated using the companion diagnostic to predict susceptibility to a bleed or an embolism while on Warfarin. This is one way in which Medco measures *"hard, real outcomes, keeping in mind clinical benefits versus economics."*

Medco is now deploying personalized medicine programs that payers and patients can sign up for. They have programs for Warfarin, Tomaxifen, Plavix, and many other drugs for which a companion diagnostic can be used. This program is a fully integrated service and includes counseling and access to the test. The service is paid for by the payer.

The Role of Industry in France

In Vitro Diagnostics

Christian Parry
Vice-President, French Syndicate of In Vitro Diagnostic Industry (SFRL)

In vitro diagnostic refers to tests performed on samples (blood, for example) in a laboratory without patient contact – this can be a public or private laboratory. Because there is no patient contact, regulation is less complicated. Furthermore, the process of in vitro diagnostics is highly automated, and batches of samples can be processed and analyzed efficiently. In France in vitro diagnostic represents about 95% of the work done in biology in the country – equivalent to about 1.7 billion Euros. 'Point-of-care' tests constitute a growing market within the industry.

While regulation of this industry may be less complicated, there is nonetheless regulation, both national and international. The Global Harmonization Task Force was created to develop "greater uniformity between national medical device regulatory systems." (**http://www.ghtf.org/**) It is working on standardizing the different protocols in biological medicine going from clinical validation to labeling.

Timelines in in vitro diagnostics are uneven: 3 to 5 years to develop a reagent, for example, that might be used for about 15 years, but during this time it will undergo several redevelopments. Innovation in in vitro diagnostics differs from innovation in academic laboratories. While academic laboratories may make discoveries in the fundamentals of biology, in vitro diagnostics makes discoveries concerning the ways drugs work. Two types of innovation characterize this work: a "rupture" with previous thinking that suddenly leads to the discovery of an entirely new diagnostic for a disease (a type of innovation much favored by the media) and, more commonly, an "incremental innovation" that redevelops new generations of tests. *"This incremental innovation represents 70% of our R&D budgets,"* Christian Parry notes.

With such a wealth of discovery coming from in vitro diagnostics, some players speak as if there is an explosion in this market. That is impossible, however, as desirable as it may be, because the cost of drug development is too great, sufficiently large cohorts of patients difficult to gather, and the cost to the public healthcare system not yet evaluated.

Medical Industry Partnerships

Catherine Lasselle

Scientific Director, the French Pharmaceutical Companies Association (LEEM)

"The medical industry is acutely conscious of its responsibility: find new treatments, bring them to physicians so they can treat patients, improve the quality of life of patients, bring new hope for cures… all this requires imagination, audacity, and tenacity." To this end, boundaries are being broken down: the artificial boundaries that previously separated academic and private research labs are falling. At the same time, we are seeing the development of a continuum between research and patient care, allowing patients to benefit more quickly from diagnostic and therapeutic innovations.

Two specific areas of innovation are worth mentioning. Medical imaging is becoming precise to the point where it will soon be possible to follow biomarkers at an infinitely minute level and to draw on nanotechnology. In the place of 'blockbuster' drugs, medical biology is discovering drugs of infinitely specific action, drugs that hold out special promises in the treatment of brain diseases – neuroprotectors, for example, that reduce brain lesions.

Along with new discoveries in the laboratories, new alliances in the board rooms are creating a changing context: alliances in the biomarker industry – pharma/pharma, pharma/diagnostics, pharma/biotech, biotech/biotech – set the stage for new R&D. In France, researchers working in medical R&D have more than doubled: today they number more than 24,000 and include 10,000 medical engineers.

Biotechnology in France

André Choulika

President, France Biotech

The progress we have made today was unimaginable 20 years ago. Then, any expert who was asked, "when will the human genome be sequenced?" would answer "2050". It was, in fact, sequenced in 2000, and the cost has decreased from several billion dollars to $10,000 for a task that takes 4 weeks to complete. Choulika predicts: *"We can envision a human genome for $1,000 in 2 or 3 years, and maybe for $300 in 5."*

Today genetic biomarkers are revolutionizing personalized medicine. It's a revolution that involves innovation in bioinformatics and robotics. But there is so much more that needs to be done. 70% of all drugs used in the world today do not target the disease molecule efficiently – it's more like carpet bombing. Personalized medicine is like a guided missile: it identifies the target, characterizes it, and attacks it. With this precision, disasters like Vioxx can be avoided. Drugs in Phase 3 or 4 of coming into the market cost up to $1.2 billion – an astronomical loss in the case of drugs that have to be recalled. The future of medical biology lies in the pairing of a companion diagnostic with a biomarker to avoid ineffective therapies and enhance effective ones.

The problem is not just getting the drug to the market – the problem is protecting the biotech company developing it. These companies are often small and young (about 8 or 10 years old). In France, the weakness of venture capital is especially harmful to these companies. From 2008 to 2009, biotech companies in financial trouble went from 40% to 47%.

"We are entering a new era: that of personalized medicine, where we do not treat a disease, we treat a patient."

The View from a Large Biotechnology and IVD Company

Christian Bréchot

Vice President of Medical and Scientific Affaires, Institut Mérieux

The road to the new era of personalized medicine is still a bumpy one. There is a great abyss between, on the one hand, the number of publications these last few years describing a biomarker that, with the appropriate clinical trials, could be the effective marker for a disease, and, on the other hand, the number of biomarkers that actually pass all the stages of development to reach the Holy Grail: a place on the pharmacy shelf.

Some of the challenges along the road include

- working in the blind: how to conduct research on a small number of molecules while keeping enough of an open mind to spot an unimaginable discovery?
- needing to combine biomarkers that are the intellectual property of different companies
- the massive cost of investing in drug development (especially for small biotechnology startups)
- the problem of trying to generate reproducible results when one is dealing with the intersection of genetics and environmental factors that cannot be controlled.

One solution that is helping at Mérieux is flexible grants: for 2 years now the company has been offering flexible grants worldwide in order to attract new concepts and to work on the threshold phase that allows a molecule to pass from concept to intellectual property and so to begin initiating the chain of events that creates a profitable new drug.

"The key for a player in this industry is to predict the difficulties that will arise for the registration of a biomarker or a drug, so as to avoid the obstacle course where one is told at each stage what the next obstacle will be."

Discussion: Negotiating Reimbursement

Given the cost of developing biomarkers and companion diagnostics, the issue of reimbursement (how much will be reimbursed and when) looms large in personalized medicine. Pierre Cassigneul offered some telling statistics regarding XDx's experience getting reimbursed in the US for AlloMap.

Out of every 100 test:

- 40 tests go to Medicare patients and are reimbursed (about $2,821) in 28 days
- 10 tests go to patients covered by Medicaid, Veterans Affairs, and other similar groups, and about half of these are reimbursed
- 50 tests go to patients with the large insurance companies in the US, and of these about 55% are reimbursed in 7 months and about 30% are never reimbursed as they are deemed by the insurer to be "experimental"

High costs and delays with regard to reimbursement in France create an even more complex landscape. Benoît Traineau (Ortho-Clinical Diagnostics) spoke frankly about trying to commercialize the Veridex companion diagnostic for breast cancer. Ortho-Clinical Diagnostics has waited 7 years for reimbursement. As a result they have slowed down their investment in the French market because *"the market conditions are not favorable. This may lead to a loss of opportunities for French patients."*

One potential boost to the pharmaceutical genomics market could come from physicians. However, their lack of familiarity with genomics has been previously noted, and there is a further complication. As Patrick Terry explained: *"Getting access to physicians is very difficult because they are busy. They are handling hundreds of patients, and finding the time to understand this technology is very hard."*

The conference was completed with an excellent overview by Professor Phillippe Amouyel (CEO, National Foundation for Alzheimer's Disease, General Director of Institut Pasteur, Lille) of the latest clinical evidence of how personalised medicine approaches can have great impact on patient outcomes with particular emphasis on Alzheimer's disease and myocardial infarction. Philippe Amouyel also presented the recent plans of Neximed, a university hospital institute, which aims to become a premier research site uncovering novel approaches in personalised medicine.

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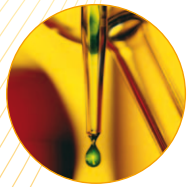
As a conclusion EPEMED's first conference highlighted the recent advances made in personalised medicine but also discussed the difficulties in making personalised treatments available for patients in France and in Europe. Alain Huriez announced that not-for-profit organization is preparing proceedings of the conference which may be downloaded from its website (**www.epemed.org**) in 2011. EPEMED is planning further events, including another international conference in 2011.

EPEMED
CONFERENCE REPORT

OPENING SESSION AND CONCLUSIONS (French)



Accueil

Dr Alain Huriez

Au nom de l'association EPEMED que j'ai l'honneur de présider, je tiens à remercier tout particulièrement Monsieur Philippe Adnot, Sénateur et Président du Conseil Général de l'Aube et membre de la Commission des finances, rapporteur des crédits de l'Enseignement Supérieur et de la Recherche, qui a bien voulu soutenir et parrainer cette conférence consacrée aux progrès de la médecine personnalisée.

Merci Monsieur le Président pour votre introduction.

Messieurs les députés, Monsieur Le Député Claude Birraux, Président de l'Office Parlementaire d'Evaluation des Choix Scientifiques et Technologiques,
Monsieur le Député et Dr Guy Lefrand, Membre de la Commission des Affaires Sociales,
Madame et Messieurs les Sénateurs,
Mesdames et Messieurs les Conseillers Référendaires de la Cour des Comptes,
Monsieur le Président de l'Université,
Mesdames et Messieurs les Professeurs,
Mesdames et Messieurs les directeurs d'organismes publics d'Etat et des ministères,
Monsieur le représentant de la Commission Européenne,
Mesdames et Messieurs les directeurs généraux d'entreprise, et présidents d'associations professionnelles,
Mesdames et Messieurs les Orateurs,
Mesdames et Messieurs, et Chers Confrères,

je suis particulièrement heureux de vous souhaiter la bienvenue à cette conférence intitulée : **la médecine personnalisée en France et en Europe, un enjeu majeur de santé et de finances publiques.** Vous découvrirez tout au long de cette journée, des présentations, tables rondes et témoignages particulièrement riches avec un point sur les progrès scientifiques et médicaux, les enjeux réglementaires, sociétaux et économiques en France, et un exemple particulièrement intéressant des applications pratiques de la médecine personnalisée aux Etats-Unis. Puis les acteurs industriels français nous parleront de la démarche de recherche et d'innovation consacrée à ce secteur, enfin nous terminerons la journée par l'accès de cette offre innovante de soins aux patients, et tirerons les conclusions avec Monsieur le Député Guy Lefrand.

Vous constaterez la participation à cette conférence de représentants de tous les secteurs, scientifique, médical, économique, institutionnel, industriel et journaliste, ceci étant d'ailleurs très représentatif de la multidisciplinarité de la médecine personnalisée et de ses impacts médicaux et économiques.

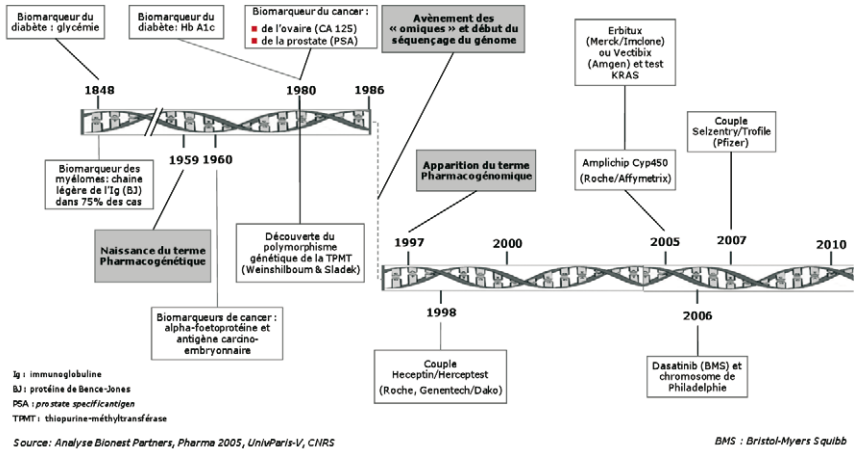
Permettez moi maintenant de passer la parole à Monsieur le Député Claude Birraux, Député de Haute Savoie, Président de l'Office Parlementaire et d'Evaluation des Choix Scientifiques et Technologiques qui nous fait l'honneur de sa présence, pour une ouverture de cette conférence et que je remercie vivement.

Session plénière

Les challenges de la médecine personnalisée, Dr Alain Huriez

Mesdames, Messieurs,

La Médecine Personnalisée et les biomarqueurs font partie des pratiques médicales depuis de nombreuses années et leur développement s'est accéléré dans la dernière décennie



Bien que le concept de la personnalisation des traitements des malades soit identifié depuis l'antiquité et que dès le 19ème siècle des avancées majeures comme le dosage de la glycémie ait permis un suivi plus adapté des malades, la **médecine personnalisée** moderne a connu un essor considérable depuis une quinzaine d'années grâce au succès des premiers biomarqueurs tumoraux qui permettent d'administrer des traitements mieux ciblés et plus efficaces.

La génomique médicale : potentiel pour une innovation majeure

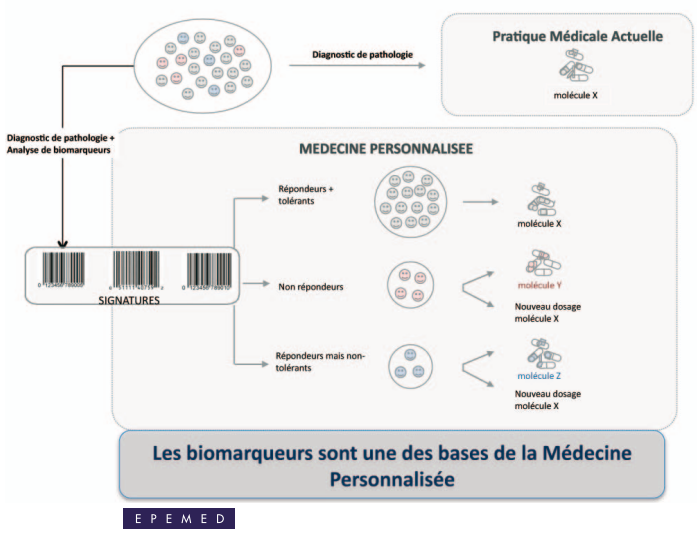
Période	Génomes	Temps nécessaire	Personnel nécessaire	Coût par génome
1990-2003	1. NIH référence 2. Celera référence	~5 ans	~5,000	~2-3 milliards US Dollars
2003-2009	10 nouveaux	~6 mois	Douzaines	300,000 ➜ 38,000 US Dollars
2010-2014	10^3-10^4	2-4 semaines	3-4*	3,800/19,500 ➜ 1,000 US Dollars
2015-2020	Millions	15 minutes	<<1	100-250 US Dollars

** hors analystes bioinformaticiens*

EPEMED

Les travaux sur le génome humain, les progrès de la biologie moléculaire, l'arrivée de nouvelles disciplines comme la pharmacogénomique, les progrès considérables constatés dans l'analyse de l'ADN, de l'ARN et des protéines, la puissance numérique au service de la bio-informatique, de la statistique ou de l'imagerie pouvant traiter des millions de données, ont transformé un concept naissant en une approche médicale multidisciplinaire à part entière, avec ses applications pratiques en thérapeutique quotidienne.
La médecine personnalisée peut se définir comme l'utilisation d'informations cliniques, génétiques ou génomiques d'un patient pour lui proposer le traitement et/ou le dosage médicamenteux le plus efficace et le plus adapté. La prise en charge médicale est ainsi pensée de manière individualisée, quand des outils diagnostiques (principalement bio-marqueur ou imagerie) permettent une optimisation du traitement en temps, quantité ou choix de la molécule administrée.

Les progrès : des traitements plus adaptés et plus efficaces



Le **biomarqueur** associé de plus en plus étroitement à la médecine personnalisée, est devenu le marqueur moléculaire multiparamétrique, l'outil de détection ou de suivi de pathologie de même que l'outil diagnostic compagnon de thérapeutique, tant il est étroitement lié à une molécule ou à son mode d'action. On doit les premiers succès médicaux et commerciaux à bon nombre d'entreprises de biotechnologie Nord Américaines, qui ont développé et commercialisé des marqueurs diagnostiques ou prédictifs de pathologie ou de réponse au traitement.
Le biomarqueur est devenu ainsi un concept familier, correspondant à de multiples définitions qu'il soit utilisé en clinique ou en recherche et développement, qu'il dépende de technologies aussi diverses pour obtenir l'information pertinente que la génomique (étude des gènes), la transcriptomique (étude de l'expression des gènes), la protéomique (étude des protéines), ou encore l'imagerie.

Le biomarqueur constitue sans nul doute la base de la médecine personnalisée du 21ème siècle.

"My physician prescribed a customized formulation for me. Here's my DNA sequence."

En tant qu'acteurs de ce domaine, notre responsabilité est bien évidemment d'apporter toutes les précisions nécessaires afin que les cliniciens, les patients, les citoyens, les autorités, mesurent les progrès actuels de cette discipline tout en ayant à l'esprit que la médecine basée sur les données de biologie moléculaire restera une composante d'une médecine et d'une offre des soins, qui continueront par ailleurs à enregistrer des progrès dans les prochaines décennies par des molécules thérapeutiques innovantes, thérapie cellulaire et génique, la médecine prédictive, les campagnes publiques de prévention, de dépistage ou de vaccination.

Notre devoir est aussi d'apporter une clarification sur les définitions des termes employés : biomarqueurs, diagnostic compagnon, médecine individualisée et d'alerter sur les risques inhérents aux tests génétiques imprécis, non validés, proposés sans le moindre contrôle médical ou réglementaire, et qui n'apporteront aucune information médicale pertinente et utile.

L'accès aux patients et aux cliniciens d'outils validés en essai clinique et fiables sera par ailleurs un élément essentiel du succès de la diffusion en pratique, de la médecine personnalisée. Il sera de la responsabilité des agences d'évaluation, réglementaire, médicale et économique d'intégrer ces nouveaux éléments dans leur activité.

Les deux tables rondes de la matinée nous permettront de faire le point sur ces questions.

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Le potentiel de la médecine personnalisée moderne a immédiatement trouvé un écho dans les communautés scientifique et médicale et chez les industriels, notamment aux **Etats Unis**, auprès des associations de patients, des sociétés savantes médicales, des systèmes de remboursement qui y ont vu des opportunités de mieux soigner, de dépenser moins ou mieux pour une prise en charge médicale optimisée des assurés. Des relais associatifs se sont créés et c'est sous l'impulsion de la Personalized Medicine Coalition (PMC), association créée en 2004, que cette révolution médicale s'est concrétisée en une réalité d'outils disponibles pour les patients : La PMC a ainsi travaillé avec celui qui n'était encore que le sénateur Barack Obama pour l'introduction du « Genomics and Personalized Medicine Act » en 2006. Ceci a favorisé l'accès au marché de ces innovations médicales.

Nous aurons le privilège d'écouter cet après-midi **Monsieur Patrick Terry,** fondateur de la PMC et un parterre d'intervenants comprenant le président de la PMC, le président d'une société de biotechnologie spécialisée dans ce domaine ou encore du représentant d'un acteur économique de premier plan, le PBM MedCo. Ces intervenants nous expliqueront comment les progrès de la médecine personnalisée et des biomarqueurs aux Etats Unis, se traduisent en une meilleure offre de soins pour le bénéfice des patients, tout en adressant la question essentielle d'une optimisation des dépenses de santé.

La France possède d'excellents atouts

- **Recherche scientifique, clinique et médicale,**
- **Mathématiciens, physiciens et statisticiens,**
- **Organismes de transfert technologique et de valorisation,**
- **Institutions publiques (Afssaps, HAS,..),**
- **Agences de soutien à l'innovation et aux programmes collaboratifs, plateformes de génétique moléculaire,**
- **Industrie pharmaceutique et diagnostique,**
- **Jeunes entreprises innovantes sur la thématique biomarqueurs et médecine personnalisée.**

La France dispose de formidables atouts dans ce domaine :

- une recherche scientifique, clinique et médicale d'excellence,
- des mathématiciens, physiciens et statisticiens de réputation internationale,
- de très bons organismes de transfert technologique et de valorisation,
- des institutions publiques (Afssaps, HAS,..) renommés pour la qualité de leurs évaluations,
- des agences de soutien à l'innovation et aux programmes collaboratifs comme l'OSEO, l'ANR et d'autres instituts.

- une industrie pharmaceutique et diagnostique extrêmement active,
- enfin un tissu de jeunes entreprises innovantes portant la thématique des biomarqueurs et de la médecine personnalisée, dont les dirigeants sont dans cette salle aujourd'hui.

Tout ceci constitue un environnement propice à assurer un leadership européen dans ce domaine.

A titre d'exemple la société TcLand Expression, essaimage de l'INSERM de Nantes, a montré la voie de la médecine personnalisée en France avec un parcours de pionnier mondial dans le domaine des biomarqueurs en immunologie. Elle fait l'objet depuis plusieurs années d'un soutien indéfectible du fonds français AURIGA, dont je salue ici les représentants.

Les marqueurs, développés et validés par la société, permettront demain l'arrêt ou la diminution des traitements anti-rejet après transplantation d'organes chez de nombreux patients, de même ses marqueurs compagnons permettront d'optimiser les traitements biologiques au long cours chez les patients souffrant de polyarthrite rhumatoïde, un des postes les plus importants des dépenses de la caisse d'assurance maladie.

Ces biomarqueurs compagnons et de médecine personnalisée protégés par une quinzaine de brevets internationaux seront demain une innovation française diffusée au niveau mondial.

Quels enjeux pour l'avenir ?

La Médecine Personnalisée se développe rapidement, notamment outre atlantique car de nombreux acteurs (chercheurs, investisseurs, industriels) mesurent dorénavant l'importance économique et médicale de cette discipline.

Les biomarqueurs sont intégrés dans toutes les étapes de la chaîne de recherche et de développement et de valeur de l'industrie.
Les publications se multiplient de la part des équipes académiques qui disposent d'outils de recherche performants et d'une recherche translationnelle organisée.
Les autorités réglementaires intègrent voire encouragent le développement de biomarqueurs pouvant avoir un impact sur la qualité ou l'efficacité des soins.

Au total il est probable que dans 15 ans, les biomarqueurs et la médecine personnalisée constitueront la base de nombreuses offres de soins, qui seront généralisées et encouragées par le corps médical et les systèmes de santé.

Dans ce contexte il faut que la France se prépare à ces progrès et qu'au-delà de ses propres atouts, plusieurs initiatives soient soutenues pour lui permettre de développer un leadership dans ce domaine en Europe.

C'est j'espère grâce à cette journée de présentations que nous pourrons mieux cerner nos atouts et les initiatives qu'il reste à soutenir pour que **la France, absente de la révolution de la biotechnologie et des anticorps monoclonaux des années 1980, ne le soit pas également des biomarqueurs et de la médecine personnalisée.**

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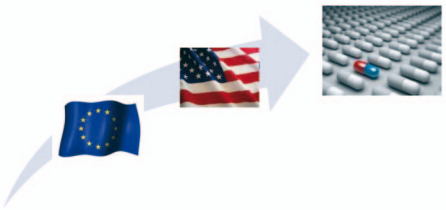
Pourquoi EPEMED ?

A l'origine de la création d'EPEMED, pour European Personalised Medicine, association européenne d'origine française, un constat simple : celui du retard de l'Europe sur les sujets de médecine personnalisée et de diagnostic moléculaire.

La Médecine Personnalisée en Europe



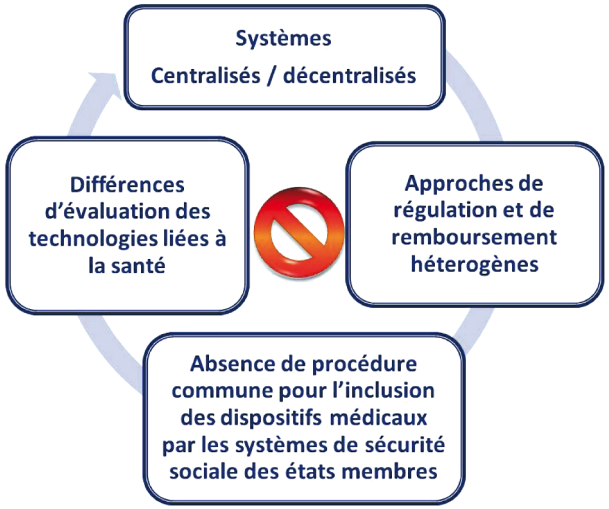
- Les applications pratiques de la Médecine Personnalisée, du diagnostic moléculaire ou des diagnostics compagnons, sont encore en retard en Europe en dépit des progrès et des premiers succès constatés aux Etats Unis.
- Des attentes importantes sont identifiées pour des meilleures formation et diffusion de l'information auprès des différents acteurs Européens, pour une plus grande compréhension des avancées de la Médecine Personnalisée, et la nécessité de rendre ces innovations accessibles au marché Européen.

EPEMED

La diffusion et la mise à disposition des outils de médecine personnalisée supposent un modèle nouveau où les environnements règlementaires et les équilibres économiques entre médicament et test de diagnostic sont amenés à des évolutions profondes.

Le premier objectif d'EPEMED est donc de combler un besoin et de proposer une structure qui s'adresse aux problématiques spécifiques de la médecine personnalisée et du diagnostic moléculaire.

Europe : les défis à surmonter



L'association EPEMED a pour objectif de développer la connaissance de ces concepts en Europe, notamment à travers la diffusion d'informations (mise à disposition de documents et de points de vue d'experts sur le site internet de l'association, séminaires de travail, conférences...). Sa mission vise également à promouvoir l'harmonisation de l'accès de la médecine personnalisée au niveau européen.

EPEMED

- EPEMED est une association à but non-lucratif, d'origine française, qui rassemble les acteurs de la Médecine Personnalisée.
- EPEMED étudie les problématiques auxquelles sont confrontés les industriels, les institutions de régulation et de remboursement de soins ainsi que les gouvernements.
- L'objectif d'EPEMED est la mise à disposition d'une plateforme de réflexions et d'harmonisation pour le développement de la Médecine Personnalisée et son implantation en Europe avec un regard particulier sur le rôle du diagnostic pour faire de la Médecine Personnalisée une réalité.

La France peut continuer à jouer un rôle de locomotive Européenne, l'initiative EPEMED à rayonnement Européen, doit être soutenue en France et en Europe.

Mesdames, Messieurs, j'espère que cette journée de conférences vous apportera un éclairage nouveau sur l'importance et les enjeux de la médecine personnalisée sur la santé et la qualité de la prise en charge médicale de nos concitoyens, et vous convaincra des efforts encore nécessaires de recherche, de financement et d'accès au marché, pour ce secteur, qui demain influencera positivement l'efficience de notre offre de soins.

Je vous remercie de votre attention et vous invite maintenant à écouter l'ensemble de nos intervenants.

Conclusions de la journée

Dr Alain Huriez

Mesdames et Messieurs,

Au nom de l'association EPEMED, permettez-moi tout d'abord de remercier tous les intervenants pour la qualité de leurs présentations, ainsi que l'ensemble de la salle pour la richesse des questions et des échanges.

Cette journée nous aura permis de retenir les points suivants :

- Le soutien politique à cette thématique exprimé par Messieurs Le Sénateur Adnot et le Député Claude Birraux, dans leur discours d'introduction.
- Une vision de la médecine personnalisée et des biomarqueurs, à la fois sur le plan scientifique, médical et de l'organisation des soins, mais aussi sur le plan réglementaire et de l'accès au marché, qui nous a permis de constater que si la France possède des atouts indéniables, beaucoup de questions demeurent sur les problématiques de l'accès au marché, de l'évaluation du couple médicament-diagnostic compagnon, de la nomenclature, du prix et du remboursement.

- Enfin nous aurons bénéficié de l'expérience américaine dans le domaine et de ce qu'il faut en retenir.
- Nous aurons par ailleurs échangé sur les thématiques du cancer, de la transplantation, de la rhumatologie, des maladies cardio-vasculaires avec des intervenants français de Paris, Nantes, Lyon, Lille, Marseille.

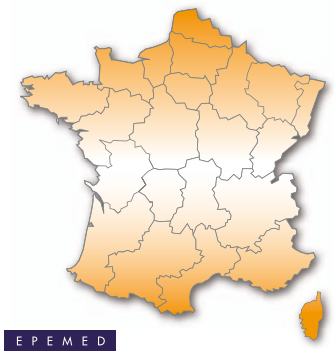
La médecine personnalisée nous concerne car c'est déjà la nôtre et ce sera demain celle de nos enfants et de nos petits enfants. Nous tous réunis aujourd'hui sommes des pionniers du domaine.

EPEMED envisage de développer un livre blanc sur cette journée, tant les débats auront été riches et porteurs d'idées et de pistes à renforcer.

En conclusion et à la lumière des débats de la journée, j'ai retenu les pistes de réflexions suivantes :

- Favoriser **l'émergence/la valorisation de projets innovants autour des biomarqueurs** en France depuis les étapes les plus fondamentales aux plus appliquées ;
- Accélérer la structuration des **centres de ressources biologiques (biobanques)** et améliorer leur accès à l'ensemble des acteurs tel que réalisé dans d'autres pays ;
- Soutenir la filière industrielle des entreprises dédiées aux biomarqueurs dans leur recherche de relais de **croissance et de moyens de financement et développement (Grand Emprunt), et d'accès au marché tels que les enveloppes STIC ;**
- Faire évoluer **le cadre réglementaire et éthique** en mettant les biomarqueurs et la médecine personnalisée au centre des préoccupations, disposer de **règles de remboursement favorables entraînant le développement de la filière des biomarqueurs ;**
- Etre à l'initiative de **l'harmonisation des procédures réglementaires et de remboursement intra-européennes ;**
- **Simplifier la réglementation** pour permettre aux sociétés de biotechnologie innovantes de développer et mettre sur le marché des biomarqueurs diagnostiques en France de ne pas être considérées comme des **laboratoires de biologie médicale**, ce qui leur interdit toute viabilité économique). **Un régime pénalisant pour les entreprises de biotechnologie françaises contrerait la politique de soutien à l'innovation mise en avant actuellement par les pouvoirs publics et affaiblirait considérablement un secteur dynamique de l'économie française face à la concurrence internationale ;**
- En fermant à la recherche médicale la possibilité d'exploitation par des entreprises qui la valorisent, la **règlementation actuelle en asséchera le financement et le développement.**

La France doit accélérer ses initiatives dans le domaine de la médecine personnalisée pour devenir un leader mondial



- Structuration des cohortes et biobanques,
- Soutenir la filière industrielle (financement et développement (Grand Emprunt),
- Premier accès facilité à son marché (STIC),
- Etre à l'initiative de l'harmonisation des procédures intra-européennes,
- Retirer de la définition de laboratoire de biologie médicale, les entreprises de biotechnologie innovantes du domaine des biomarqueurs.

Mesdames, Messieurs,

La France peut jouer un rôle majeur dans le domaine de la médecine personnalisée en Europe : soutenons les initiatives et les pistes de réflexion.

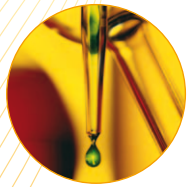
Merci encore pour votre participation.

Bonne fin de journée et bon retour.

Merci.

EPEMED
CONFERENCE REPORT

PRESS RELEASE
(French)



Communiqué de presse

EPEMED, l'association Européenne pour le développement de la Médecine Personnalisée, a organisé sa première conférence au Palais du Luxembourg

PARIS (France), le 20 Octobre 2010 - EPEMED, l'association pour le développement de la Médecine Personnalisée, une organisation européenne à but non lucratif qui rassemble différents acteurs du domaine de la médecine personnalisée, a organisé le 12 Octobre dernier, sa première grande conférence privée au Palais du Luxembourg à Paris, sur le thème de **« La Médecine Personnalisée en France et en Europe : un enjeu majeur de santé et de finances publiques »** sous le parrainage de Monsieur Philippe Adnot, Sénateur et Président du Conseil Général de l'Aube, membre de la Commission des finances, rapporteur des crédits de l'Enseignement Supérieur et de la Recherche.

L'ouverture des débats a été faite conjointement par le Député Claude Birraux, Président de l'Office Parlementaire d'Evaluation des Choix Scientifiques et Technologiques et le Docteur Alain Huriez, Président et fondateur d'EPEMED.

L'audience de cette conférence était composée de personnalités politiques et membres de hautes institutions de l'Etat, organismes publics et agences, Présidents d'Université, représentants de la Commission Européenne, ainsi que des organismes de remboursement, chercheurs, industriels et présidents d'associations professionnelles dans le domaine de la santé. Plusieurs industriels américains étaient présents et certains d'entre eux sont également intervenus, de même qu'un représentant d'un « Pharmacy Benefit Manager » actif dans le domaine de la médecine personnalisée, ainsi que le Président de la « Personalized Medicine Coalition » américaine.

Les présentations, tables rondes et témoignages avec un point sur les progrès scientifiques et médicaux, les enjeux réglementaires, sociétaux et économiques en France, et l'exemple particulièrement intéressant des applications pratiques de la médecine personnalisée aux Etats-Unis ont permis des débats riches et constructifs, sur les atouts de la France dans ce domaine et les efforts restant à accomplir, notamment sur l'accès au marché, la prise en compte de la valeur apportée par les diagnostics dans le remboursement ou encore la réglementation portant sur le statut des jeunes sociétés innovantes de diagnostic qui réalisent des tests moléculaires complexes dans leur propre laboratoire.

Cette journée fera l'objet d'un livre blanc dont les conclusions seront disponibles sur le site **www.epemed.org**. Cette conférence aura ainsi apporté un éclairage nouveau sur l'importance et les enjeux de la médecine personnalisée sur la santé et la qualité de la prise en charge médicale des concitoyens et aura convaincu des efforts encore nécessaires de recherche, de financement et d'accès au marché pour ce secteur, qui demain influencera positivement l'efficience de l'offre de soins.

« Il m'apparaît que la médecine personnalisée peut être une voie vers l'amélioration de nos dépenses de santé, dans la mesure où les investissements qui peuvent y être faits sont susceptibles d'être couverts par les économies engendrées pour la collectivité. Il est impérieux que nous passions, tous domaines confondus, à un mode d'évaluation systématique de l'efficacité de la dépense publique » a indiqué Monsieur le Sénateur Adnot.

« Il est probable que dans 15 ans, les biomarqueurs et la médecine personnalisée constitueront la base de nombreuses offres de soins, qui seront généralisées et encouragées par le corps médical et les systèmes de santé. Dans ce contexte il faut que la France se prépare à ces progrès et qu'au-delà de ses propres atouts, plusieurs initiatives soient soutenues pour lui permettre de développer un leadership dans ce domaine en Europe » a ajouté le Dr Alain Huriez, président d'EPEMED.

A propos d'EPEMED : EPEMED est une organisation à but non lucratif créée en 2009. L'association a été fondée afin de traiter les problématiques de la médecine personnalisée auxquelles sont confrontés les différents acteurs du domaine en Europe, notamment les autorités réglementaires, les payeurs et les assureurs. La mission d'EPEMED consiste à offrir une plateforme destinée à harmoniser le développement et la diffusion de la médecine personnalisée à travers l'Europe, en mettant l'accent sur le rôle fondamental des diagnostics, afin de transformer la médecine personnalisée en réalité. L'organisation est dirigée par un groupe dynamique et diversifié de leaders du domaine de la médecine personnalisée, qui comptent une vaste expertise dans l'application et la mise au point d'outils de diagnostic visant à proposer de meilleurs soins aux patients.

À propos de la médecine personnalisée : Les innovations récentes du diagnostic moléculaire ont joué un rôle important dans l'amélioration de la prise en charge de patients souffrant d'un certain nombre de pathologies. Les thérapies personnalisées et les diagnostics compagnons forment ensemble le domaine de la médecine personnalisée, dans lequel les informations cliniques, génétiques et environnementales d'une personne sont utilisées pour choisir plus précisément les médicaments et les doses pour chaque patient en particulier. Il est attendu que l'application de la médecine personnalisée améliore les soins aux patients tout en réduisant les dépenses de soins de santé.

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Pour plus d'information sur EPEMED veuillez consulter www.epemed.org ou contacter :

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