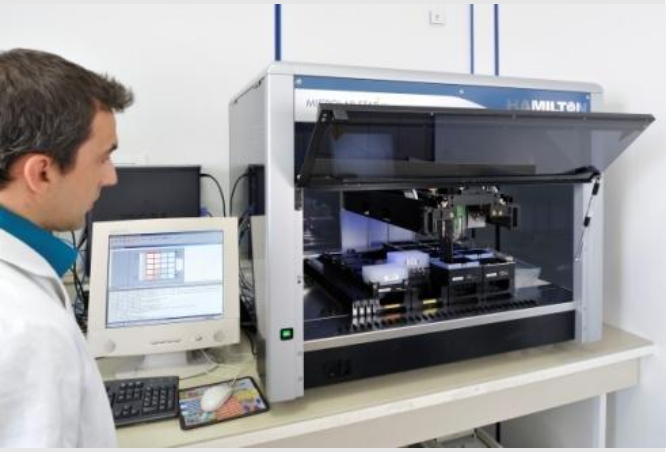


INTEGRAGEN

TECHNOLOGICAL OPPORTUNITIES AND INNOVATIONS TO IMPROVE EPILEPSY DIAGNOSIS AND MANAGEMENT – THE ROLE OF SMEs

European Forum on Epilepsy Research

Dublin 2013

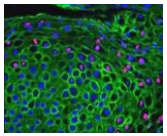
Emmanuel Martin
Director Genomics Services

IntegraGen Overview

IntegraGen has built a wealth of in-house expertise in the analysis of genomic data and biomarker identification, which supports all the Company's operations, spanning molecular diagnostic development and genomic services

Core Expertise

Overview



- **Core expertise in clinical genomics, biomarker discovery and molecular diagnostics**
- **Wide ranging experience in study protocol planning, bio-informatics and analysis**

Operations

Oncology Diagnostics

- Development and sale of biomarker based tests for targeted oncology therapies
- Colorectal and Hepatic Cancer tests in late stage trials
- CE mark expected by 2H 2013 for both tests

Autism Diagnostics

- Development of tests for the genetic markers of autism
- CLIA-lab test approved in the US
- Ongoing patient trial to support 2013 launch of a non-familial test with a large potential market

Genomic Services

- The expert in leading edge Genomic technology platforms
- First French commercial lab to offer a range of High Throughput Sequencing, Genotyping and Bioinformatic systems
- Advanced wet and dry lab facilities in Evry, Paris

IntegraGen,

A SME IMPLICATED IN GENETICS OF EPILEPSY:

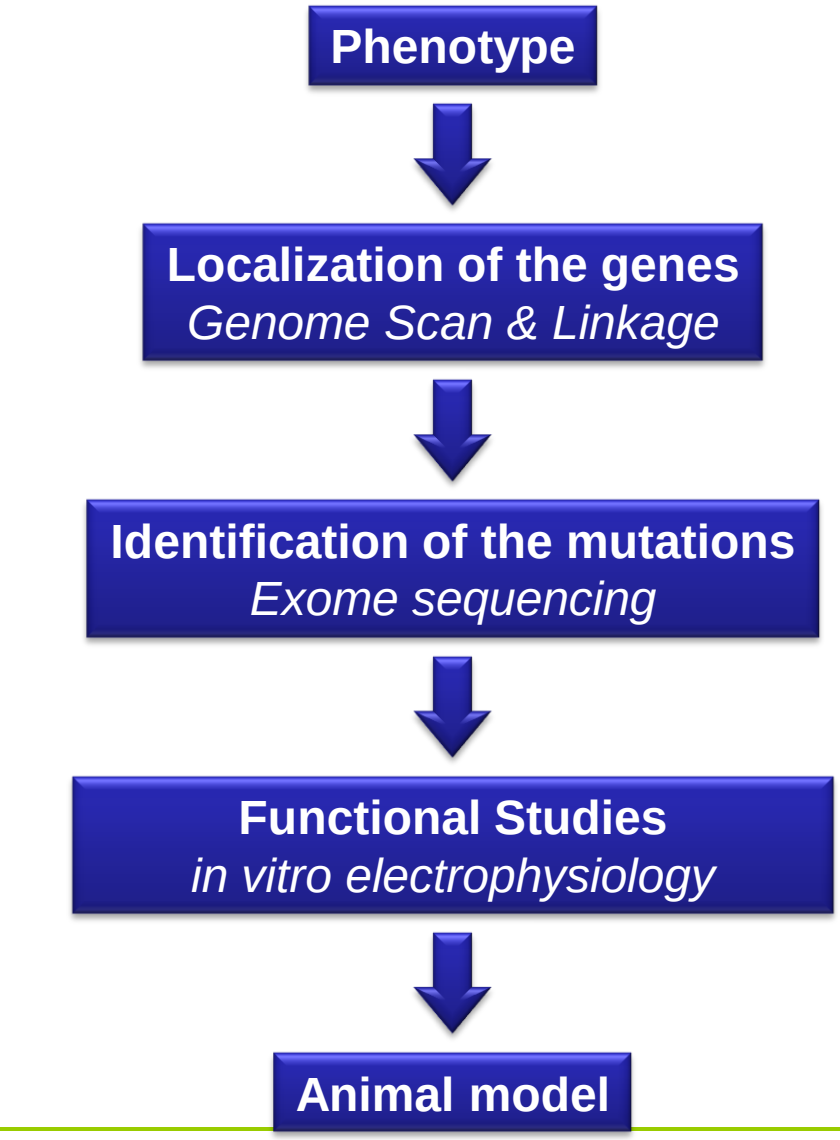
A SUPPORT OF RESEARCH FOR ACADEMIC LABORATORIES

Epilepsies and Genetics

- 3 underlying causes: Genetic, Structural-metabolic, Unknown cause
- Genetic epilepsies represent 40 % of epilepsies
- Most genetic epilepsies have a complex inheritance
- Rare forms with autosomal dominant/recessive transmission

Major Aims: identification of new molecules

well known strategy….



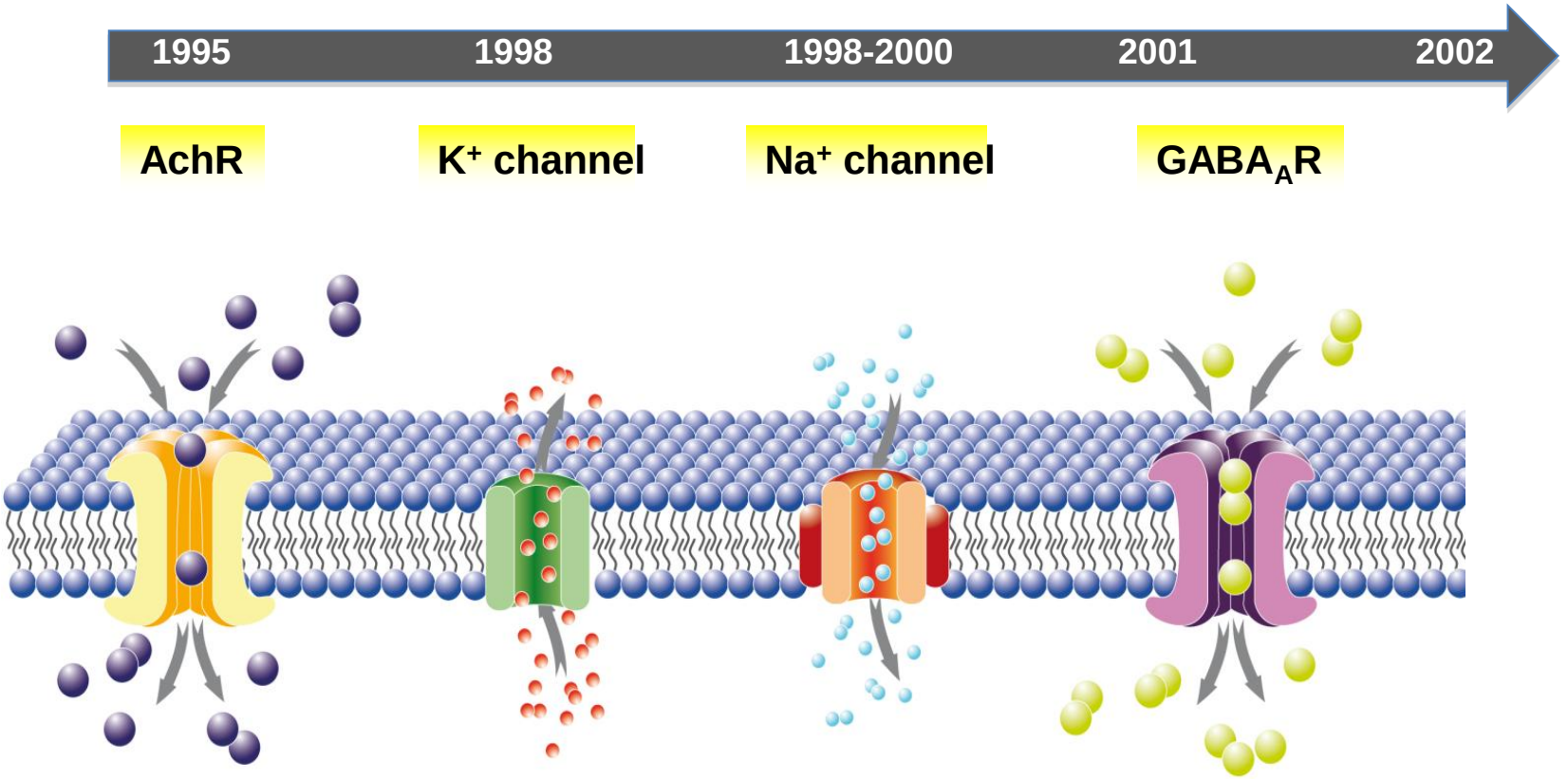
IntegraGen

IntegraGen

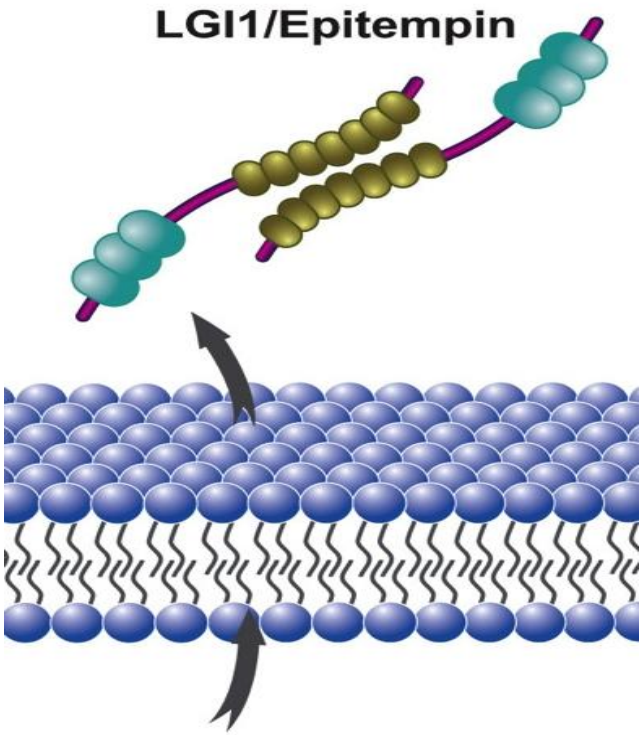
Academic labs

Academic labs

The majority of epilepsy genes encode ion channels



But not only channelopathies…



[Secreted protein]

Kalachicov et al, Nat Genet (2002)

And More Recently

Nat Genet. 2013 Apr 26;45(5):552-5. doi: 10.1038/ng.2601. Epub 2013 Mar 31.

Mutations of DEPDC5 cause autosomal dominant focal epilepsies.

Ishida S, Picard F, Rudolf G, Noé E, Achaz G, Thomas P, Genton P, Mundwiller E, Wolff M, Marescaux C, Miles R, Baulac M, Hirsch E, Lequern E, Baulac S.

1] Institut National de la Santé et de la Recherche Médicale (INSERM) U975, Institut du Cerveau et de la Moelle Epinière (ICM), Hôpital Pitié-Salpêtrière, Paris, France. [2] Université Pierre et Marie Curie-Paris 6 (UPMC), Paris, France.

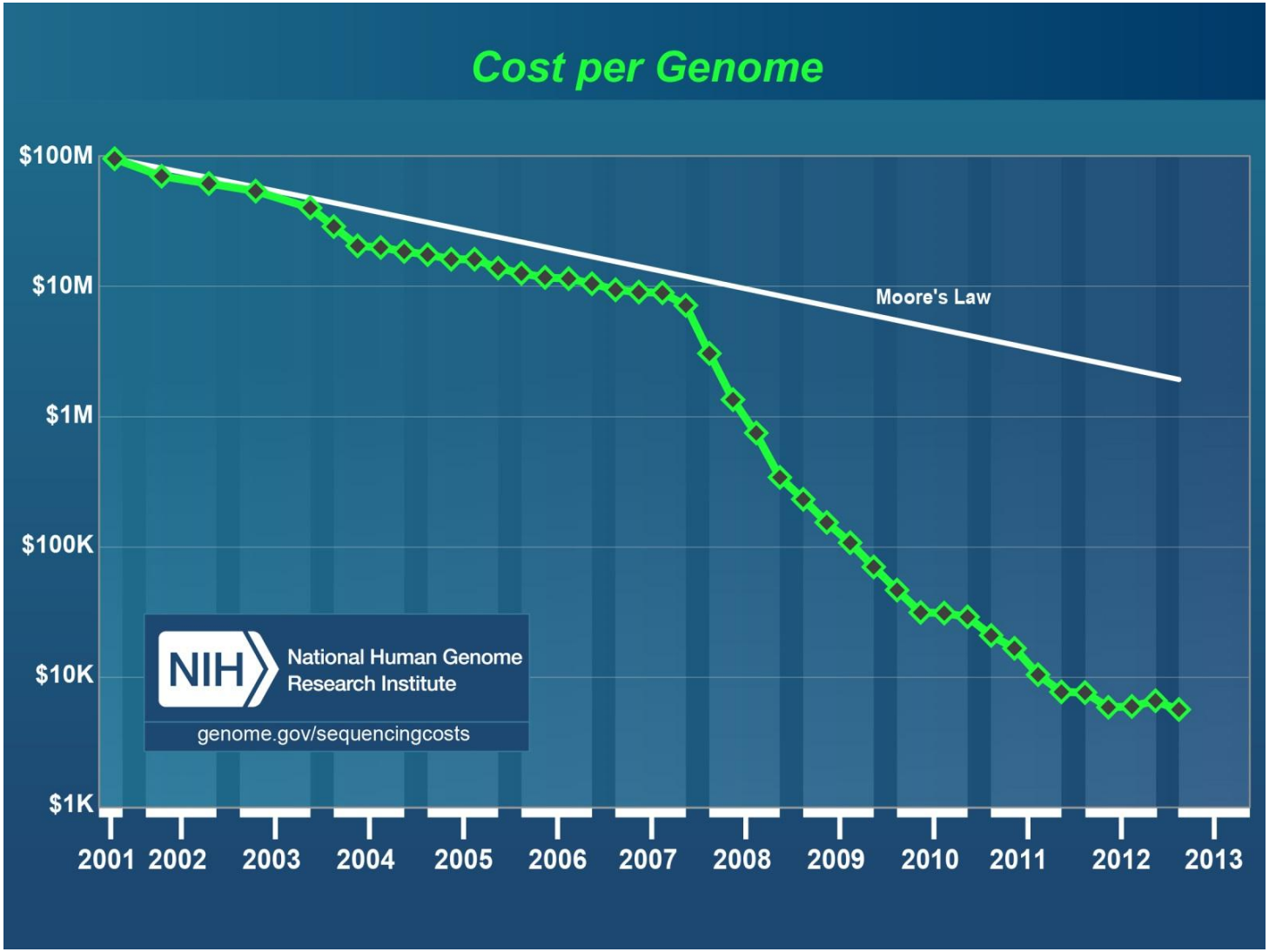
DEPDC5 does note encode a channel subunit

Highly conserved gene, Broadly expressed, No known partners

New pathway involved in epileptogenesis

NEW PHARMACOLOGICAL TARGETS

We are at the beginning of the story



A SME as a service provider

- **By proposing access to cutting edge technologies**
  - And tools helping the interpretation

We are close to the 1k€ genome but still at the 1M€ interpreteome

- **Delivering high quality data, on time**

- **In a collaborative mode more than in a furnisher/customer relationship**

Can we do more ?

IntegraGen,

A PARTNERSHIP FOR MOLECULAR DIAGNOSIS ?

A SME as a co-developper ?

- Is there some IP, even co-owned with the partners?
- Is there a niche market to explore ?
- Is our expertise an added value for the project ?
- Is it granted, even partially ?

MOLECULAR DIAGNOSIS IN SEVERE EPILEPSY (1)

EPILEPTIC ENCEPHALOPATHIES (EE):

- Pharmacoresistant epilepsy
- Cognitive delay, autism
- Neurological signs

GENETICALLY DETERMINED

MUTATIONS SHALL BE FOUND

GENETIC COUNSELLING PART OF THE PATIENT MANAGEMENT

MOLECULAR DIAGNOSIS IN SEVERE EPILEPSY (2)

EE : MORE THAN 100 GENES INVOLVED

Development of high throuput sequencing methods needed:

- **Targeted genes-capture / sequencing (Kit / ready-to-use assays)**
- **Whole Exome Sequencing**
- **Whole Genome Sequencing**

Collaboration & partnership between SMEs and advanced medical experts are crucial to set up the best strategy

Importance for a SME to maintain cohesion in the development

Epilepsy and Autism are frequently associated

- **Prevalence of Epilepsy in Autism : 5 to 40 %**
  - 0,5 to 1% in the general population, varies upon autism subtype, age, mental retardation, associated neurologic disorder…
- **Prevalence of Autism in Epilepsy : 5 to 30 %**
  - 1/150 in the general population

We probably could take adantage from a common knowledge

Canitano, 2007, Eur Child Adol Psy
Berg et al, 2011, J Chil Neurol

Conclusion (1)

- New genomics approaches, and sequencing capabilities are key in disease understanding but also in diagnosis and patient management
- SMEs like IntegraGen act as a support for research but also in tools and kits development for clearly identified market
- 30 % of commune epilepsies are pharmacoresistant. Better knwoledge of genes and pathways involved shall lead to new targets indentification and personalised treatments.

Conclusion (2)

There is many other areas where implication of SMEs is as important for the diagnosis and patient management in epilepsy

- **Seizure detection devices**
- **Softwares and smartphone applications (patient management)**
- **Microelectrodes …**

Thanks to Pr Eric Le Guern and Dr Stéphanie Baulac

Thank you for your attention