Innovative Medicines Initiative
Personalised Medicine
Cancer and Diabetic
Research

Krakow Biotechnology congress - 13 October 2011

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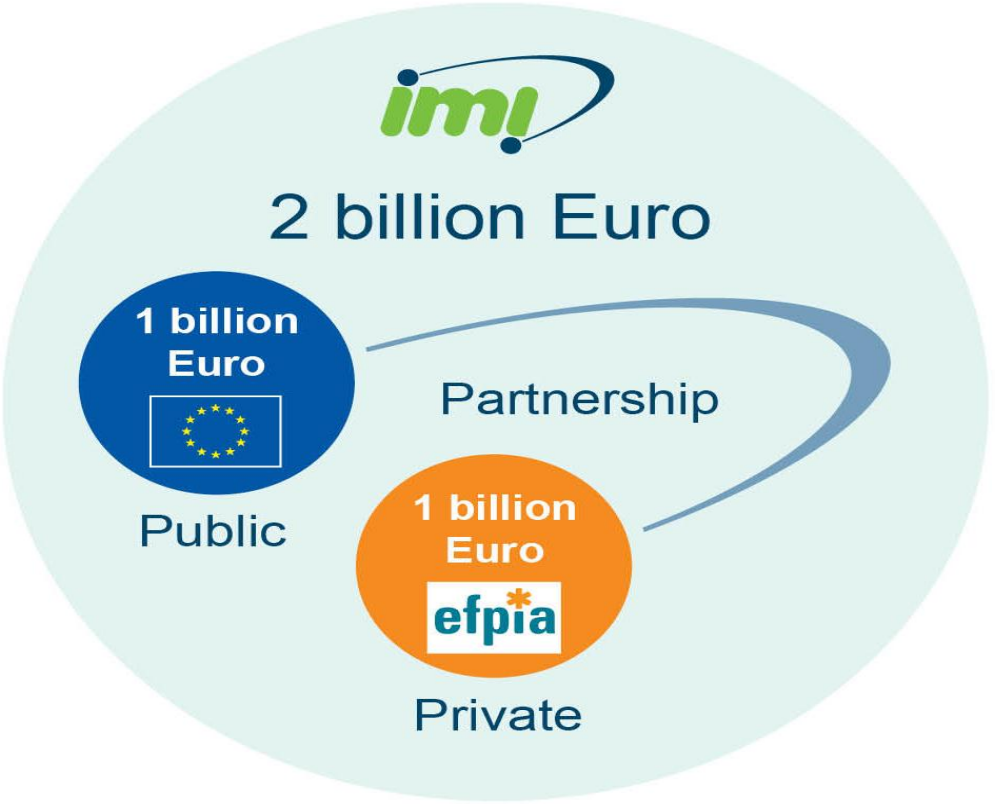
What is the Innovative Medicines Initiative?



A Largest PPP in life science R&D in the world focused on needs common to industry and patients. Unique in scope and ambition From basic research to pharmacovigilance

Why is IMI needed?

- Drug R&D is become increasingly complex, expensive and time consuming
- The number of new drugs (new molecular entities) for patients is declining
- Europe is loosing ground in global pharmceutical R&D

Open Innovation in the Pharmaceutical Sector

Foster open collaboration between all stakeholders, e.g. industry, academia, patients organisations, public authorities (including regulators), clinical centres, etc.

Modernize drug development via new approaches, methods and technologies, better use of research results and data, and more skilled staff

Support 'pre-competitive pharmaceutical research and development', in order to accelerate the development of safer and more effective medicines for patients.

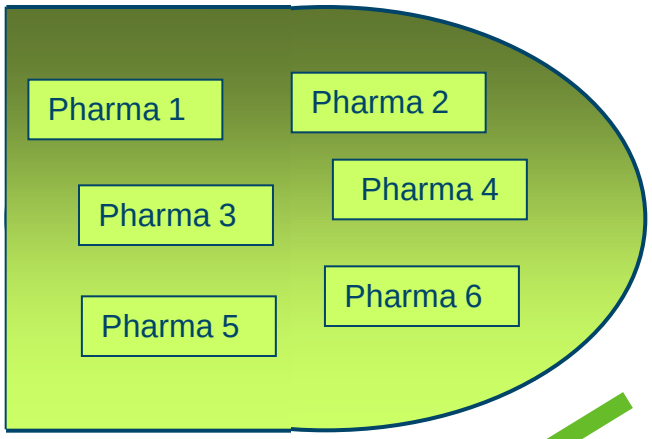
Key Concepts

- Non-competitive research for EFPIA companies
- Competitive calls for IMI beneficiaries
- Open collaboration in final consortia

Key Deliverables of Non-Competitive Research

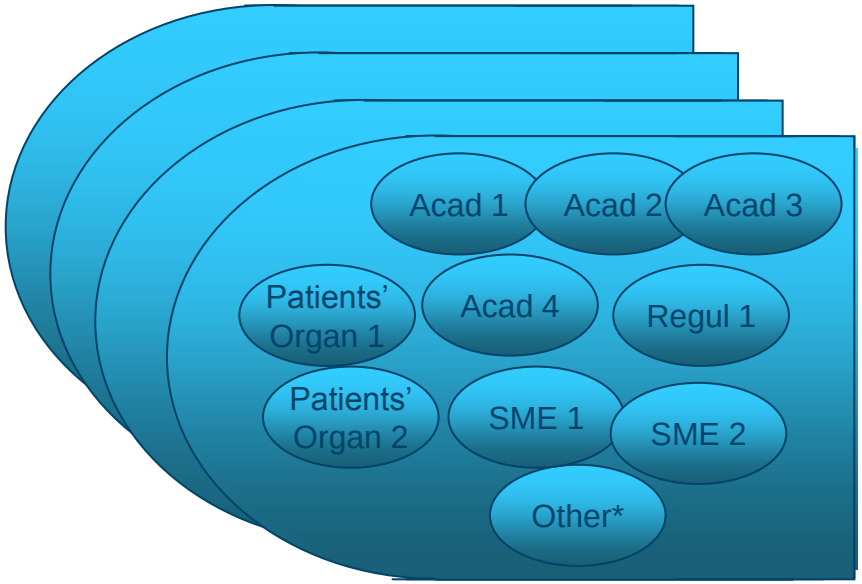
- Establishment of common databases
- New tools for identification of drug targets, manufacturing and delivery
- Standardization and harmonization of models and assays for drug efficacy and safety (*biomarkers*)
- Patient reported outcomes
- New classification of diseases

Building an IMI consortium



Step 1:

A set of **EFPIA** companies **define a topic** on which they commit to collaborate

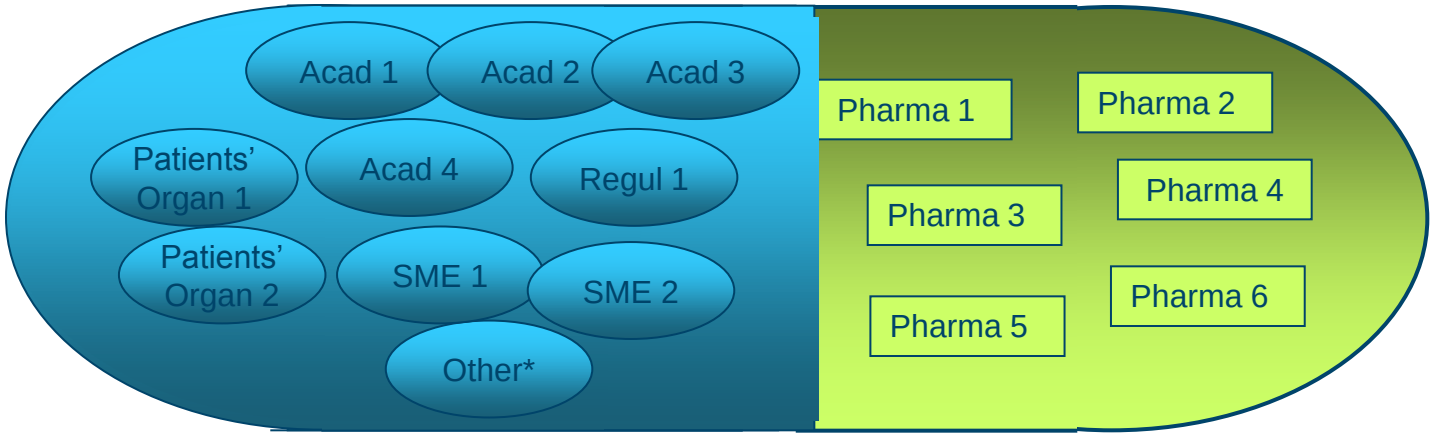


Step 2:

Consortia eligible for EU funding **compete** through Expressions of Interest which are **ranked** by independent experts

Step 3:

The top-ranked EU-fundable consortium joins the EFPIA companies to **form the final consortium** which develops the **full proposal**, subject to peer-review before final approval



Calls 1 & 2: consolidated figures

	Call 1	Call 2	Total
Projects	15	8	23
EFPIA Companies	21	21	23
Academic teams	195	103	298
SME teams	24	23	47
Patients' organisat.	9	2	11
Total Budget (M€)	281	172	453

Patients' Organizations in IMI Projects

- Int. Alliances of Patients' Organizations
- Alzheimer's Europe
- Eur. Genetic Alliances' Netw.
- Genetic Interest Group
- European AIDS Treatment Group
- European Lung Foundation
- Int. Primary Care Resp. Group
- British Lung Foundation
- Asthma UK
- Lega Italiano Anti-Fumo
- Dutch Asthma Foundation

Involvement of Regulatory Agencies

- Partners of consortia, supported by EU funding
  EMA, MHRA (UK), DKMA (DK), AEMPS (SP), SwissMedic (CH), AFSSAPS (FR)
- Members of Project Advisory Boards (FDA, EMA)
- IMI Scientific Committee Observer
- Definition of IMI priorities for future topics

Innovative Medicines Initiative
Personalised Medicine
Diabetic Research

Diabetes – why is it a key focus in IMI?

- Pandemic disease of the 21st century
  - 2010: 285 million people worldwide
  - 2030: 439 million people worldwide

    (in particular spreading to the younger population)

Key bottlenecks addressed within IMI: 1rst Call Projects

- Diabetic Treatment Shift (enable cure) – IMIDIA
- Diabetic Complications – SUMMIT
- Diabetic Heterogeneity – DIRECT (IMI 3rd Call Project)

IMIDIA consortium

imidia. European combined excellence in diabetes research | Landscape*

To develop novel means to assess, to predict and to prevent beta-cell demise as well as to restore normal beta-cell mass and function for the treatment of diabetes

21 Partners

- 8 EFPIA companies
- 12 Public organisations
- 1 SME

efpia

IMIDIA addresses key bottlenecks for the development new therapies

- **Novel tools** for the study of:
  - human beta-cell development, function and survival
  - human beta-cell functional modulation by potential therapeutic compounds
  - in vivo beta-cell imaging
- **Biomarkers:**
  - for the diagnosis and prognosis of beta-cell failure
  - for monitoring diabetes progression and treatment
- **Knowledge:**
  - on novel pathways and sites that control beta-cell proliferation, differentiation and apoptosis
  - on the role of nutrient-regulated pathways in controlling beta-cell mass and function

Finally! A human pancreatic β cell line

Gordon C. Weir and Susan Bonner-Weir

Section on Islet Cell Biology and Regenerative Medicine, Research Division, Joslin Diabetes Center, and Department of Medicine, Harvard Medical School, Boston, Massachusetts, USA.

Related Commentary, page 3395

Technical advance

A genetically engineered human pancreatic β cell line exhibiting glucose-inducible insulin secretion

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Diabetic Complications

Diabetic nephropathy

About 30% of T1D and T2D patients develop DN. This is characterized by a progressive decline of kidney function (can lead to need for dialysis or transplantation).

Diabetic retinopathy

Affects most patients with DM to some degree and 2% will become blind.

There is visual impairment in most of the patients.

Cardiovascular Diseases

Up to 75% of all deaths in T2D are due to CVD. T1D patients have a 4 to 7 fold risk of major

CVD, T2D patients a 2 – 4 fold risk for a development of MI, stroke or peripheral arterial diseases.

There is a high therapeutic need for new treatments of diabetic complications beyond glucose lowering therapies.

The development of ways, technologies and tools to make clinical trial testing of novel medications in diabetic complications shorter and more focused.

SUMMIT

surrogate markers for micro- and macro-vascular hard endpoints for innovative diabetes tools

19 Partners

- 4 EFPIA companies
- 18 Public organisations
- 1 SMEs

SUMMIT achievements

- Identified and implemented highly sophisticated **software tools** to select samples that are maximally informative when analyzed. Performed literature mining on proteins, lipids and metabolites and also identified strategies for predictive models of diabetes complication. The new IT systems will increase the speed, accuracy and effectiveness of the research.

- **Clinical studies** aiming to identify non-invasive markers of vascular injury have started in patients. These patients are also undergoing genetic and non-genetic biomarker testing.

- Existing **animal models** of diabetes that replicate various aspects of macro- and micro-vascular complications have been selected and are being characterized further.

- Criteria for **definition of vascular complications** have been established and methods for non-invasive evaluation of disease progression in small animals validated.

The Innovative Medicines Initiative – a public private partnership to promote European diabetes research (Diabetologia, in press)

IMI 3rd Call

Personalized Medicine in Diabetes

DIRECT
Dlabetes REsearCh on patient straTification

Future of Diabetes Treatment: Personalized Medicine

Where is the heterogeneity in T2DM ?

- **Bottleneck: Predictive Biomarkers**
  - Predict incident of diabetes
  - Predict rapid deterioration of glycaemia
  - Assess underlying beta-cell function/mass
  - Predict response/non-response to therapy

→ **Identify/collect cohorts of extreme phenotypes (rapid deterioration /non-deterioration of glycaemia, response/non-response to therapy)**

Need for IMI Personalized Medicine Collaboration

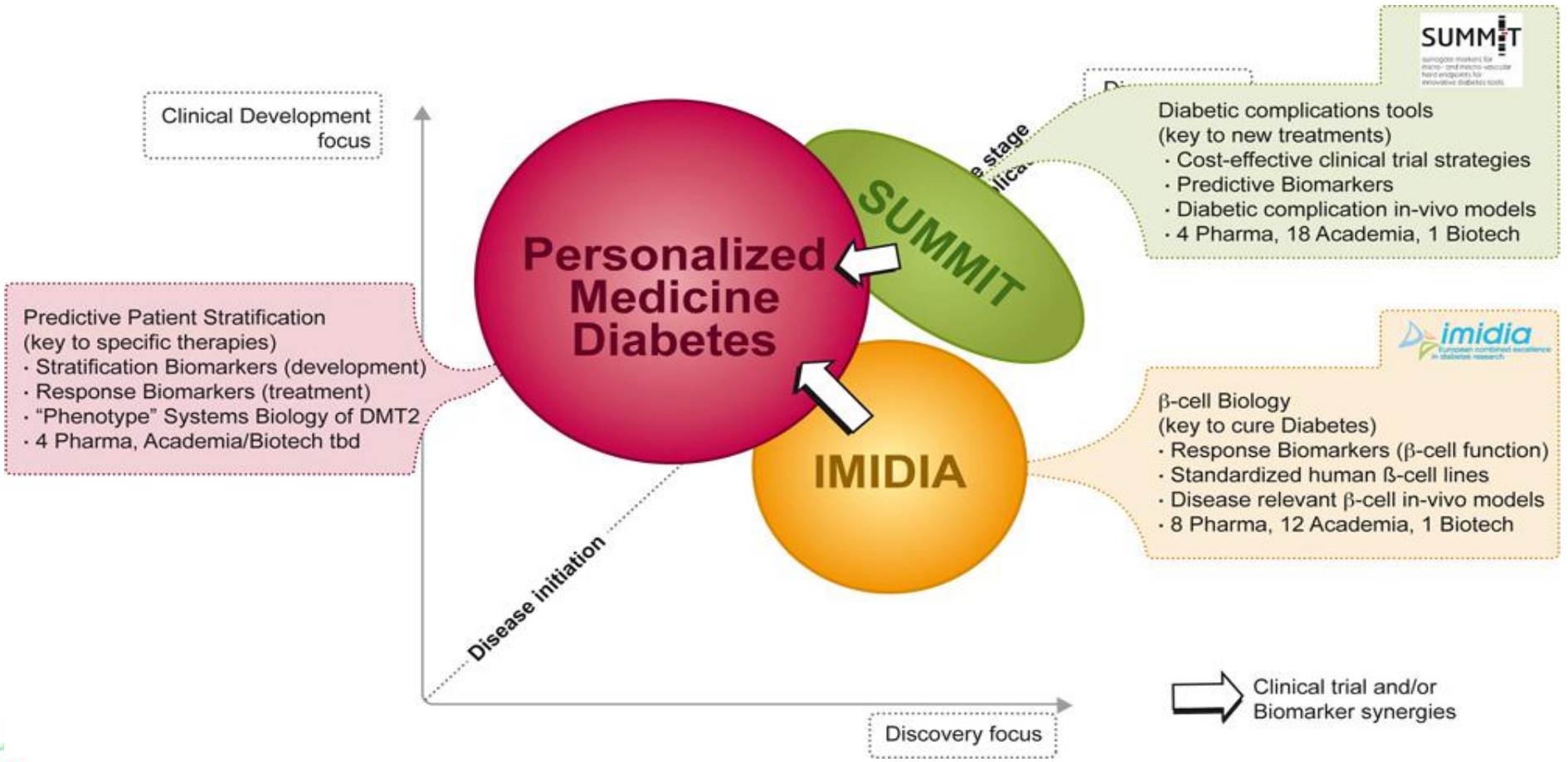
- Topic to complex for a single company / institute
  - Access to well characterized cohorts
  - Access to a broad range of technologies (‚omics ‘)
  - Access to a large European data base for ‚System Biology ‘
- Biomarker validation in prospective large ‚non- compound development‘ clincial trial

Key Deliverables

- High quality European data bank with phenotypical data sets.
- Systems Biology Platform: Integrating clinical data, biological data, genomics, metabonomics and other relevant data.
- Development of novel data mining tools and algorithms to generate stratification and response biomarker candidates
  - **To predict incident diabetes**
  - **To predict rapid deterioration of glycaemia**
  - **To assess underlying beta-cell function/mass**
  - **To predict response/non- response to therapy**

- Development of ‘Industrialized’ Biomarker Assays
- Prospective Clinical Trials: Validation of biomarker candidates
- Assessment of the response (or lack of response) to established therapies (for instance incretins) in well defined sub-populations.

Diabetes – addressing key bottlenecks with a portfolio of projects



IMI 2nd Call for Proposals: Oncology Call Topics

New Tools for Target Validation to Improve Drug Efficacy

Molecular Biomarkers – Accelerating and Refining Cancer Therapy Development

Imaging Biomarkers for Anticancer Drug Development

IMI 2nd Call for Proposals: Oncology Call Topics

1. **Delivery of care to cancer patients is a major health need across the EU**

2. **There is consensus among the EFPIA companies active in the field regarding the unique challenges in cancer drug discovery and development**

   - **Disease heterogeneity: intra- and inter-patient variability**
   - **Genetic instability of tumours and development of drug resistance**
   - **Advances in genomic technologies support the paradigm of "personalized medicine**

   The 3 projects presented here have a broad range, addressing the key research issues

PREDECT: NEW MODELS FOR PRECLINICAL EVALUATION OF DRUG EFFICACY IN COMMON SOLID TUMOURS

The PREDECT consortium consists of

8 EU institutes

3 SMEs

7 EFPIA members

PREDECT: NEW MODELS FOR PRECLINICAL EVALUATION OF DRUG EFFICACY IN COMMON SOLID TUMOURS

Objectives of the Project

The development of improved *in vitro* and *in vivo* models with greater predictive capacity for the human disease to support target identification and target validation.

1: Development of complex *in vitro* cellular models for the validation of potential drug targets and their cross-validation with well characterized *in vivo* models of disease pathology

2: Integrated bioinformatics evaluation of multivariate data in order to generate testable hypotheses (= systems biology approaches)

PREDECT : Key Deliverables

- **Key Deliverables are:**
  - **Development and validation of a new generation of *in vitro* and *in vivo* models with greater predictive capacity for the clinic.**
    - Alignment of models with molecular profiles obtained from high quality human tumour samples to assess their relevance and applicability.
    - Establishment of the limits of manipulability of the new, complex model systems for target validation and drug testing using new methods and technologies.
  - **Systems biology descriptions of tumour biochemical processes in novel models**
    - Capable of describing the context of novel targets in human tumours and generating hypotheses to be tested in models of target validation.

OncoMark:
Methods for systematic next generation oncology biomarker development

The OncoMark consortium consists of

- 8 Academic partners
- 3 SMEs
- 8 EFPIA partners

OncoMark: Objectives of the Project

Development of innovative approaches for biomarker assessment in

The peripheral circulation in order to assess the potential of

- **Circulating tumour cells,**
- **Cancer stem cells**
- **and/or Nucleic Acids**

As a surrogate for invasive biopsies.

1: Identification and qualification of markers predictive of response to therapy

2: Investigation of circulating tumour cells and nucleic acids as potential biomarkers

- **3: Investigation of cancer stem cells as potential biomarkers**

OncoMark: Key Deliverables

- **Innovative, sensitive, specific and accurate methods to detect biomarkers**
- **Qualified biomarkers that advance our understanding of tumour heterogeneity**
- **New sensitive, specific and accurate methods to detect and characterize circulating tumour cells**

Why QuIC-ConCePT?

Quantitative Imaging in Cancer – Connecting Cellular Processes to Therapy

The QuIC-ConCePT consortium consists of:

- 14 Academic partners
- 1 SME
- 7 EFPIA partners

QuIC-ConCePT: Imaging Biomarkers in Cancer

- Already decision-making in drug development >50 years
  - TNM, RECIST, FDG-SUV, DCEMRI k^{trans}, cardiac safety

- However many published imaging biomarkers are not yet decision-making
  - *"if I see no effect on the imaging biomarker, should I stop developing this drug?"*

  - QuIc-ConCePT to qualify Imaging Biomarkers
  - cell death, proliferation, apoptosis
  - invasion, metastasis

QuIC-ConCePT : Project Objectives

1. To qualify IBs of tumour cell :
- proliferation,
- apoptosis,
- Necrosis,

that will allow drug developers to reliably demonstrate the modulation of these pathologic processes in tumours in patients in cancer clinical trials.

2. To devise, evaluate and introduce IBs of invasion and metastasis.

What is special in Research in IMI ?

- Integrated strategy
- Comprehensive picture for bottlenecks
- Broad patient relevance
- Highly networked and collaborative

IMI CALL 4 TOPICS

Medical Information System

1. A European medical information framework (EMIF) of patient-level data to support a wide range of medical research
2. eTRIKS: European translational information and knowledge management services

Chemistry, Manufacturing and Control

3. Delivery and targeting mechanisms for biological macromolecules
4. In vivo predictive biopharmaceuticals tools for oral drug delivery
5. Sustainable chemistry – Delivering medicines for the 21st century

Technology and Molecular Disease Understanding

6. Human induced pluripotent stem (hiPS) cells for drug discovery and safety assessment
7. Understanding and optimising binding kinetics in drug discovery

Human Induced Pluripotent Stem Cells in Drug Development

- hiPS are promising tools for the development of innovative medicines:
  - Drug discovery
  - Drug safety

- Need for public/private collaborative research to:
  - Establish biobanks
  - Access hiPS cell lines from different ethnicities and patients with defined phenotypes/genotypes
  - Establish standardised biological assays
  - Establish collaborations with other consortia

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