Public-Private Translational Research on Rare Diseases

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Rare Disease Research: The Need for Innovative Approaches

- Rare diseases represent a significant public health issue and a priority for European programs in public health
  - ≈ 30 million patients in the EU-27
  - Lack of treatment options
  - Council Recommendation of 8 June 2009 on an action in the field of rare diseases

- Despite the high quality of public research and the existence of centres and networks of excellence in rare disease research, there is a lack of innovative translational approaches for the development of new drugs.

- “Translational Gap” can be filled by public-private collaborations including academics and partners with expertise in innovative drug discovery (industry-biotechs-SMEs)
  - state of the art approaches: high throughput screening, advanced medicinal chemistry
CNCCS: An Example of Public-Private Cooperation in Translational Research

- Public-Private Non-for-Profit Consortium
- Created in 2010
- Funded by Italian Ministry for Research and Education
About IRBM Science Park

- Located on the outskirts of Rome
- Former Basic Research site of Merck Research Laboratories (1990-2009)
- Reopened in February 2010 under new private ownership
- Broad spectrum of Drug Discovery research services
- Participate in collaborative research projects
On-Site Joint Ventures

- **CNCCS**: Public-private consortium, partnership with Italian National Research Council (CNR) and National Institute of Health (ISS)
  - National Compound Collection and Screening Center
  - Research Center for Rare and Neglected Diseases

- **Advent**: GMP Production Facility for Adenoviral Vectors

- **Promidis**: discovery stage company, focused on finding disease-modifying therapies for protein aggregation disorders
Full Program Support

- Highly integrated, automated and optimized processes
- Medicinal and Peptide Chemistry*
- Assay development and screening
- Biology-Pharmacology-DMPK

*former Merck Center of Excellence for Therapeutic Peptides
Strengths

- Former Big Pharma Discovery Site
- Highly qualified multidisciplinary staff
- Track Record of innovative drug discovery
- State of the art lab equipment
- Optimized processes, operational excellence
Track record

- **Isentress (raltegravir):** First-in-class HIV integrase inhibitor
  Winner of the Prix Galien USA 2008 as Best Pharmaceutical Agent

- **MK-5172:** first reversible pan-genotypic HCV protease inhibitor
  Completed phase 2 trials

- Contribution to the development of **Zolinza (SAHA):** first-in-class HDAC inhibitor for the treatment of cancer

- **>20 preclinical candidates,** including antiviral and anticancer drugs that achieved proof of concept and are currently undergoing advanced clinical studies.
High Skillset and International Experience

30% Study/Work Experience Abroad
>15 Scientific papers/person
>4 Patents/person
Growth of IRBM Science Park

Reached Break-even in 2011
Partners, collaborators and customers
About CNCCS

- Public-Private Non-for-Profits Consortium
- Created in 2010
- Funded by Italian Ministry for Research and Education
Mission

- Establish a National/European collection of chemical compounds
- Identify novel probes and leads through High Throughput Screening
- Establish a Drug Discovery Research Center for Rare, Neglected and Poverty-Related Diseases
Major Activities

- Compound repository and nearly 100k compound collection
- HTS campaigns leading to the identification of several novel leads
- Filed patent applications on novel treatments for malaria and beta-thalassemia
- Established important national and international scientific collaborations
- Membership in European research infrastructures
Drug Discovery and Development

- Target Identification
- Lead Identification
- Lead Optimization
Collaborative Hub & Spike Model

Neglected Disease experts

Target Identification

Rare Disease experts

Disease Foundations

Clinical Research

Compound Collection – Lead Identification – Lead Optimization

Organic Chemists

Animal Models

Bio-Informatics
Collaborators

- University of Padova
- University of Siena
- University of Ferrara
- University of Genova
- University of Cagliari
- University of Rome Tor Vergata
- University of Rome La Sapienza
- CISI scrl
- Exiris srl
- University of Melbourne
- University of Maryland
- Institut Pasteur Paris
- Columbia University
- Swiss Tropical and Public Health Institute
- Sanford-Burnham Medical Research Institute
- Medicines for Malaria Venture
Collaborative Projects

- Obesity/diabetes
- Hepatitis C Virus infection
- Cardiomyopathies
- Malaria
- Trypanosomiasis
- Hemoglobinopathies
- Muscular Dystrophy
- Galactosemia
- Rare cancers
National Compound Collection

- Launched call for compound contribution: Sent to >600 Italian chemists from CNR, ISS, Universities
- Established procedures for reception, quality control and storage
- Started collecting compounds from public and private contributors
- In-house design and synthesis of chemical libraries
- Collection expected to reach 100k compounds in 2013
Compound Collection: Repository

- Current capacity 200k, expandible to 500k
- Fully automated storage under controlled atmosphere
- Acoustic nanodispensing into assay microplates
- Robotic systems for High Throughput Screening (HTS)
Beta-thalassemia research

- **Rare** hereditary hemoglobin disease, causes anemia

- Defect in beta-globin production

- Can be corrected by re-expression of gamma-globin (fetal Hb)

- Current treatment: blood transfusion
Lead Optimization: Inducers of Fetal Hemoglobin

**Gamma-Globin Induction in erythroid cells**

**Induction of HbF in erythroid precursors from beta-thalassemic patients**

- **Untreated**
- **+drug**

Patent filed
Contact

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Malaria Research

- Malaria, caused by *Plasmodium* parasites, is one of the most devastating poverty-related diseases: 90% of deaths in sub-Saharan Africa

- Malaria kills nearly one million people (mostly children) each year and causes more than 500 million clinical cases.

- The number of deaths due to malaria doubled in the two decades preceding the millennium, primarily due to the spread of parasite resistance to antimalarial drugs.
Discovery of Novel Antimalarial Agents

- Specific Inhibitors of *Plasmodium falciparum* histone deacetylase (PfHDAC) generated through screening and lead optimization

- Selective killing of *plasmodium* vs. human cells

- Reduced toxicity

- Antiparasitic effect in *plasmodium*-infected mice

- Patent filed
EU-OPENSSCREEN

European Infrastructure of Open Screening Platforms for Chemical Biology

- accelerate the discovery of biologically active substances in all areas of Life Sciences
- harness the rich chemistry knowledge of Europe in a common compound collection
European Infrastructure for Translational Medicine

• Client driven, non-profit organization comprising European academic centers of excellence in translational research

• EATRIS partner institutes provide support in bringing innovative ideas for novel preventive, diagnostic or therapeutic products towards first in human application and on to clinical proof of concept