Macro Regional Innovation Week
Opening Research Infrastructures to Industry
Thursday 29th September - Trieste

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The **ICGEB** provides a scientific and educational environment of the highest standard and conducts innovative research in life sciences and **biotechnology** for the benefit of developing countries. It strengthens the research capability of its Members through training and funding programmes and advisory services and **represents a comprehensive approach to promoting biotechnology internationally.**
ICGEB Policy Guidelines on Patents, Licensing, Copyrights and other Rights to Intellectual Property

One of the basic objectives of the ICGEB is "to promote international co-operation in developing and applying peaceful uses of genetic engineering and biotechnology in particular for developing countries", "to develop and promote the application of genetic engineering and biotechnology for solving problems of development, particularly in developing countries", and "to assist developing countries in strengthening their scientific and technological capabilities in the field of genetic engineering and biotechnology" (Article 2(a), (d), (c) of the Statutes);

Towards the fulfillment of Its objectives, The ICGEB shall in Particular "carry out research and development including pilot-plant activities in the field of genetic engineering and biotechnology", "carry out a programme of bio-informatics to support in particular research and development and application for the benefit of developing countries", and "maintain close contacts with industry" (Article 3(a), (h), (j) of the Statutes).

The means for the practical achievement of the objectives of ICGEB are twofold: on the one hand the publication of all results of its research activities is mandatory, "provided such publication does not contravene its general policy regarding rights to intellectual property approved by the Board", on the other hand "patent and other rights, and any financial or other benefits associated herewith" shall be used (Article 14(1), (5) of the Statutes).

Adopted by the Board of Governors under Article 6(2)(e), (8) of the Statutes, at its 7th session (New Delhi, 13-14 November 2000)
Traslational Research (+70 patents)

Human Health:
- Vaccines (i.e. Malaria, Dengue)
- Diagnostics (i.e. virology, genetic diseases)
- Therapy (i.e. drugs, cell therapies)

Agriculture and food:
- Crop improvement (i.e. bio-inoculants, drought resistance);

Environment:
- Bio-remediation

Energy:
- Bio-fuels
Biotechnology transfer

The transfer of technologies is one of the most relevant activities of ICGEB. Over 70 agreements have been concluded with industrial partners located in Argentina, Brazil, China, Cuba, Egypt, India, Iran, Pakistan, Russia, South Africa, Sri Lanka, Syria, Turkey, United Arab Emirates, United States of America, Uruguay and Venezuela.

The procedure to transfer ICGEB technologies foresees the finalization of a Technology Transfer Agreement, which usually provides for a period of training in the ICGEB laboratories by a number of industrial partners' employees, a supply of genetically modified strains and the protocols for the production, purification and quality control of a specific biotechnological product.

**Products**
- Recombinant Human Erythropoietin
- Recombinant Human Interferon α2a
- Recombinant Granulocyte Colony Stimulating Factor
- Recombinant Human Insulin
- Recombinant Human β Interferon 1B
- Recombinant Human Interferon α2a and Pegylation of IFN α2a
- Recombinant Granulocyte Colony Stimulating Factor and Pegylation of rhG-CSF
- Recombinant Hepatitis B Surface Antigen (R-HBsAg)
The ICGEB network of Member States: challenges and opportunities
• DENV is transmitted by *Aedes* mosquitoes;
• People with Dengue disease can have mild flu-like symptoms, but can lead to lethal complications (sever Dengue);
• Recent estimate indicate 390 million Dengue infection/yr on the rise, of which 96 million clinically relevant. Half of the human population is at risk.

• No specific treatment, recent vaccine partially protective;
• 4 distinct serotypes of the virus (DENV1-4). Recovery from infection by one provides lifelong immunity against that particular serotype. However, cross-immunity to the other is only partial and temporary. Subsequent infections by other serotypes increase the risk of developing severe dengue.
• Approximately 5,000–13,000 TBE cases/year.
• Most cases occur from April through November, with peaks in early and late summer when ticks are active.
• The incidence and severity of disease are highest in people aged ≥50 years.

• Endemic Central Europe and Asia.
• Three sub-types: Far Eastern, Siberian and Western European.
• TBEV geographical distribution is expanding.
• Vaccine available (Western strain), no drugs.
• WNV can cause a fatal neurological disease in humans. However, approximately 80% of people who are infected will not show any symptoms;
  • WNV is mainly transmitted to people through the bites of infected mosquitoes.

• The virus can cause severe disease and death in horses.
• Vaccines are available for use in horses but not yet available for people.
• Birds are the natural hosts of West Nile virus.
ZIKV is transmitted primarily by *Aedes* mosquitoes;
People with Zika virus disease can have mild symptoms (fever, skin rash, conjunctivitis, muscle and joint pain, malaise or headache) for 2-7 days;

- There is no specific treatment or vaccine available;
- Complications include paralysis (Guillain-Barré syndrome) and microcephaly in babies born from infected mothers;
- Sexual transmission has been reported.
Time course of viraemia, antibody production and the diagnostic protocols for flaviviruses

Viremia

IgM

IgG

2-3 weeks

months

years

time

Virus isolation
RT-PCR
NS1-ELISA

IgG-ELISA
IFA
HI assay
PRNT

MAC-ELISA
IFA
HI assay
AVIRNITA
ArboVIRus Network between NIgeria and ITAly

Establishment of a reference laboratory for Arbovirus infection surveillance at the WHO/ITD Laboratory, University of Maiduguri Teaching Hospital, Borno State, NIGERIA (Head: Professor Marycelin M. Baba)

ACHIEVEMENTS
- Implementation of virological assays (IgM/IgG ELISA, RT-PCR, PRNT);
- Exchange of knowhow and researchers;
- Survey of Arbovirus sero-prevalence in 310 suspected febrile Malaria and Typhoid patients in Nigeria;

REFERENCES
POC testing for resource-limited settings

“Accurate diagnostics have the potential to affect health care decisions to a degree well out of proportion to their cost. It has been estimated that diagnostics account only 2% of the cost of health care, but affect 60-70% of treatment decisions. In resource-limited settings, the impact of diagnostic tests that can be provided at the immediate point-of-care (a point-of-care test, or POCT) is potentially even greater, because the alternative to a POCT may be no diagnostic support at all”.

Bringing the lab to the patient: developing POC diagnostics for resource-limited settings. A report from the American Academy of Microbiology (2011).

WHO criteria for the ideal diagnostic test ASSURED: Affordable, Sensitive, Specific, User-friendly, Rapid and Robust, Equipment-free (or minimal) and Deliverable to end users.

Development of POCT devices @ICGEB LMV

OBJECTIVE
To develop (at the prototype level first) a multiparametric point-of-care test (POCT) for the diagnosis of flavivirus infection based on a **bio-CHIP** and the associated **Reader Unit**.

PROJECTS
- **DIA-OLED**: development of an *organic light emitting diode* (OLED)-based bio-CHIP and the associated Reader Unit for the detection of nucleic acids;

- **CHIP-OLED**: development of an OLED-based bio-CHIP and the associated Reader Unit for the detection of human antibodies;

- **FLAVIPOC**: development of a label-free bio-CHIP for antigen and antibody detection during flaviviral infection.

RESULTS
- Development of a **POCT device for the amplification of nucleic acids (PCR)**.

- Development of **two POCT devices for the identification of antigens and antibodies**.
DIA-OLED: development of an organic light emitting diode (OLED)-based bio-CHIP and the associated Reader Unit for the detection of viral nucleic acids

- Peltier for thermal cycling with a 8 mm hole
- PDMS chip with 2 twin channels that fit in the 8 mm hole of the Peltier;
  - Thickness 600 μm;
  - Chamber volume 2 μl (total 7 μl)

National R&D project financed by Regione Friuli Venezia Giulia (art. 12, DM 593/2000, € 1.788.540) in collaboration with Plast-Optica Spa, Eurotech Spa, Euroclone Spa, Alphagenics Srl and University of Trieste.
CHIP-OLED: development of an OLED-based bio-CHIP for the detection of human antibodies

- Emission filter
- Fluorescent anti-human antibody (AlexaFluor 430)
- Human serum antibody
- Viral capture antigen
- Glass/polystirene
- Excitation filter

hTG2 antigen x3
BSA x1

a = 0.5 mg/ml (5 ng/spot)
b = 0.1 mg/ml (1 ng/spot)
c = 0.02 mg/ml (0.2 ng/spot)


CHIP-OLED PROJECT

International R&D Project financed by FP7 ERA NET in collaboration with OREL (Slovenija), Cosylab (Slovenija), Laplace-CNRS (France), LED Engineering (France).
FLAVIPOC: development of a label-free bio-CHIP for antigen and antibody detection

### Viral antigens

- **NS1**
- **Envelope E**

### Recombinant antibodies

- **ZIKV**
- **TBEV**
- **WNV**
- **DENV3**

**Positive α-Env TBE selected clones**

- H5
- H7
- B8
- F10

**E = Cell Extract**

**SN = Surnatant**

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**FLAVIPOC Regional Project from the Regione Friuli FVG (PAR FSC 2007-2013) in collaboration with Euroclone SpA, ICGEB, University of Trieste, CBM and Burlo Garofolo Children Hospital.**
Reflective Phantom Interface (RPI)® enables the detection of biomolecules in water-based fluids (serum, plasma, tears, saliva).

When light hits the interface between distinct media, a reflected beam is generally produced, when a low reflection material is used, a particular condition is obtained, in which even a small number of molecules that stuck at the interface will produce a substantial variation in the reflected light. The reflectivity of the spots gives a direct, quantitative and real-time measurement of the amount of captured target molecules, and thus of their concentration in the investigated solution. Detection based on spots enables the simultaneous label-free measurement and quantitative analysis of dozens of molecular targets.

Giavazzi et al. PNAS 2013
FLAVIPOC: development of a label-free bio-CHIP for antigen and antibody detection
A mobile smartphone-based prototype

Docking station with no active components. All operations are performed by the smartphone hardware (LED, CCD, Wi-Fi connection) and software (image acquisition, data analysis, user interface).

Giavazzi et al. Biosensors & Bioelectronics, 2014
Internet of Things
Collection, integration and processing of data

POCT
Diagnostic Labs
Vector surveillance
Animal reservoir surveillance

Outbreak management
Risk maps
Information
Prophylaxis
INTERREG V-A Italy-Slovenija 2014-2020 (proposal)

VIS – Surveillance and response to merging arboviral infections in the trans-border region.

University of Trieste – IRCCS Burlo
Sorveglianza diagnostica delle Arbovirosi

International Centre for Genetic Engineering
and Biotechnology (ICGEB)
Test diagnostici Innovativi

CBM scrl
Hub per le imprese

Region Veneto – Direzione Prevenzione,
Sicurezza Alimentare e Veterinaria
Sorveglianza sanitaria del territorio

University of Lubiana – Faculty of Medicine
Sorveglianza diagnostica delle Arbovirosi

Institute Nazionale di Sanità Pubblica - Lubiana
Sorveglianza sanitaria del territorio

University of the Litoral – Capodistria
Sorveglianza dei vettori
THANK YOU

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