NEXT-GENERATION DIAGNOSTIC PLATFORMS: SMART INTEGRATION OF CONVERGENT SCIENCES & TECHNOLOGIES

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www.bdi.ie

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OUTLINE

• Profile of the BDI

• Trends in POC Diagnostics

• Key Issues: Overview of Presentations
BDI PROFILE

• Industry-Academic-Clinical Partnership
• Point of Care Diagnostics (Human & Veterinary)
• Team of ~120
• Distinctive Features:
  – Embedded Industry Researchers
  – Focus on Convergent Sciences & Technologies
  – Innovative Platforms
  – Translational Research
## Clinical Collaborators (Ensuring Clinical Utility!)

<table>
<thead>
<tr>
<th>Clinician</th>
<th>Specialty</th>
<th>Hospital</th>
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</thead>
<tbody>
<tr>
<td>Dr. James O’Donnell</td>
<td>Blood Coagulation</td>
<td>National Centre for Hereditary Coagulation Disorders, St. James Hospital, Dublin</td>
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<tr>
<td>Prof. Dermot Kenny</td>
<td>Cardiology</td>
<td>Clinical Research Centre, Beaumont Hospital, Dublin</td>
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<tr>
<td>Prof. John O’Leary</td>
<td>Oncology (Ovarian, Cervical)</td>
<td>The Coombe Women’s Hospital, Dublin</td>
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<tr>
<td>Dr. Richard Costello</td>
<td>Respiratory Medicine</td>
<td>Beaumont Hospital, Dublin</td>
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<tr>
<td>Dr. Robert Montgomery</td>
<td>Hematology</td>
<td>The Blood Center of Wisconsin, USA</td>
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BDI VISION

- Providing **clinical utility** by advancing the **science & technology** of diagnostics to address unmet healthcare needs:
  - Early warning of major diseases (cardiac, cancer)
  - Enabling **self**-management of health
  - Establishing **personalised** therapeutic regimens (companion diagnostics)

- **Focus areas:**
  - Point of Care (POC)
  - Low Resource Environments
  - **Self Test** - Home Use
Cardiovascular Disease

Critical Problem:
Accounts for ~ 35% of all deaths
No electricity
No running water
No sanitary facilities
>45% HIV seroprevalence in the antenatal clinic
THE SCIENTIFIC CHALLENGES

‘pM concs in μL volumes of physiological fluids: ~10⁶ molecules in sample’

- High Sensitivity
- Small volumes of complex fluids
- Smart, rapid, miniature systems

Integration of diverse technologies
STRATEGIC PRIORITY AREAS

- Translational Nanomedicine
  - High-Brightness Nanoparticle Labels
  - Plasmonic enhancement of Fluorescence
  - Combined imaging & targeted drug delivery

- Ambient Assisted Living for Ageing Population
  - Breath Monitoring for COPD
  - Heart Failure Monitoring – NTproBNP biochip

- Personalised Medicine / Companion Diagnostics
  - e.g. POC Test for Platelet Function; Anti-platelet therapy

- Developing World applications / Global Diagnostics
  - Cell phones for remote diagnostics:
    - e.g. CD4 cell-counting
High Brightness Nanoparticles
Encapsulate many thousands of dye molecules inside a single NP.
Create an “Ultra-bright” label for assays

60nm diameter
Sandwich assay NIR dye doped NPs

- goat anti-human IgG polyclonal antibody
- human IgG
- labelled goat anti human IgG
  - Cy5
  - NIR-dye doped NP's
Sandwich assay Ru dye doped NPs

Human IgG sandwich FLISA with goat anti-hIgG Ru-NP conjugate 15/5/07

Best Result so far: 25 times decrease of the LOD
**Plasmonic Nanoparticles: Synthetic Capabilities**

- Capability of synthesising Ag & Au nanoparticles, nanorods, nanodiscs, prisms, core/shell nanoparticles.

  ![Nano-prisms](image1)
  ![Nano-plates](image2)
  ![Nano-rods](image3)
  ![Silver core/Silica shell](image4)

- Ability to tune excitation and emission properties by controlling the size and shape of the nanoparticle.
ACHIEVEMENT II: Plasmon enhanced assay

**Graph:**
- Fluorescence vs. hIgG (ng/mL)
- Comparison between 149 nm NPs and no NPs

<table>
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<tr>
<th>Label</th>
<th>149nm NP</th>
<th>Cy5</th>
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<tbody>
<tr>
<td>Fmax</td>
<td>142.4</td>
<td>52.51</td>
</tr>
<tr>
<td>LOD (ng/ml)</td>
<td>0.184</td>
<td>5.84</td>
</tr>
<tr>
<td>CV% (F₀)</td>
<td>4.333</td>
<td>8.723</td>
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ACHIEVEMENT II: Plasmon enhanced assay

Best Reduction in LOD
~ 30 TIMES

<table>
<thead>
<tr>
<th>hIgG (ng/mL)</th>
<th>Fluorescence [a.u.]</th>
</tr>
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<tbody>
<tr>
<td>0.01</td>
<td>0.1</td>
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<tr>
<td>1</td>
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<tr>
<td>10</td>
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- Fmax: 142.4
- LOD (ng/ml): 0.184
- CV% (F₀): 4.333
- LOD (ng/ml): 52.51
- CV% (F₀): 8.723

Antibodies Detection
Antigen Capture
Metal NPs Polyelectrolytes
Substrate
Synthesis of fluorescent magnetic nanoparticles

- Dual-function
  - Magnetic properties
  - Fluorescent properties
Åmic Open Lateral Flow (OLF) chip

www.amic.se

J&J Ortho-Clinical Diagnostics

ZEONOR (COP)
Heart Failure: NTproBNP assay on SAF scanner

- Spotting of capture antibody in on chips with removed pillars
- Synthetic samples (recombinant NTproBNP in PBS with BSA)
- Linear response in clinical range

![Raw data](image)
Platelet Function Assays

Platelets are tiny blood ‘cells’ 2-4 μm in diameter:
150,000 to 300,000 in 1ml of blood

Inappropriate formation of blood clots leads to heart attack and stroke
Imaging & Flow system for Platelet Research
OBJECTIVE

Develop a device that measures platelet function under conditions that occur in the vascular system
Overview of Session Presentations

• *Decentralization: Is there an unmet need for POC tests and pHealth lab tests?* [Hansson]

• *Truly personalised medicine! Novel population-based approaches to clinical decision-making* [Dacso]

• *Technical challenges and business case for POC assays.* [Borch/Karlsen]
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VRI Brno, CZ

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