How to get involved or start your own INRG Database Research project

Wednesday, September 22, 2021

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<th>US ET</th>
<th>BST</th>
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<td>16:00</td>
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Welcome
Introduction

Meredith Irwin
-on behalf of INRG Strategy Development Committee
- https://inrgdb.org/get-involved/
Your hosts

<table>
<thead>
<tr>
<th>Name</th>
<th>Email Address</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meredith Irwin</td>
<td><a href="mailto:meredith.irwin@sickkids.ca">meredith.irwin@sickkids.ca</a></td>
</tr>
<tr>
<td>Lucas Moreno</td>
<td><a href="mailto:lucas.moreno@vhebron.net">lucas.moreno@vhebron.net</a></td>
</tr>
<tr>
<td>Mark Applebaum</td>
<td><a href="mailto:mapplebaum@peds.bsd.uchicago.edu">mapplebaum@peds.bsd.uchicago.edu</a></td>
</tr>
<tr>
<td>Lieve Tytgat</td>
<td><a href="mailto:g.a.m.tytgat@prinsesmaximacentrum.nl">g.a.m.tytgat@prinsesmaximacentrum.nl</a></td>
</tr>
<tr>
<td>Wendy London</td>
<td><a href="mailto:Wendy.London@childrens.harvard.edu">Wendy.London@childrens.harvard.edu</a></td>
</tr>
<tr>
<td>Suzi Birz</td>
<td><a href="mailto:suzi@uchicago.edu">suzi@uchicago.edu</a></td>
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https://inrgdb.org/
## Agenda

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<tr>
<th>Topic</th>
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<th>Duration</th>
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<tbody>
<tr>
<td>Welcome and Introductions</td>
<td>Meredith</td>
<td>5 minutes</td>
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<tr>
<td>Summary of existing projects</td>
<td>Meredith</td>
<td>5 minutes</td>
</tr>
<tr>
<td>Introduction to INRG data dictionary</td>
<td>Meredith</td>
<td>5 minutes</td>
</tr>
<tr>
<td>How to frame your research</td>
<td>Mark</td>
<td>20 minutes</td>
</tr>
<tr>
<td>How to start your proposal</td>
<td>Lucas</td>
<td>5 minutes</td>
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<tr>
<td>List of potential projects</td>
<td>Lucas</td>
<td>10 minutes</td>
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<tr>
<td>Q&amp;A</td>
<td>Lieve</td>
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<tr>
<td>Closing remarks and next steps</td>
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<td>2 minutes</td>
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Summary of existing projects

Meredith Irwin
INRG Projects in Process

• INRG Research Projects (https://inrgdb.org/research/)
  • Consensus statements/papers
    • INRG risk classifier, biomarkers
  • Data mining clinical/translational projects
    • >35 approved; see website

• Examples of ongoing projects
  – Identifying neuroblastoma drivers and bringing them to the clinic
  – Gender as a prognostic indicator in neuroblastoma
  – INRG v 2.0
Introduction to the INRG Data Dictionary

Meredith Irwin
INRG Data Dictionary

- Multiple clinical factors and biomarkers, outcome
- Details for each variable in presentation on INRG website
  - Important to review to determine feasibility for projects
What data are available in INRG Database (2021)?

**ARE AVAILABLE**
- Clinical and biological factors collected in data dictionary include:
  - Age, stage (INSS/INRG), race, year
  - Primary and metastatic sites
  - Status of MYCN, 1p, 11q, 17q
  - DNA index, histology features
- Treatment categories; trial arm assigned
- Genomic Data (eg TARGET)- links
- Scans (limited, MIBG)
- Soon: digital path

**NOT AVAILABLE**
- Details of actual treatment received/delivered (only assigned treatment recorded)
- Surgical outcomes/details
- Response data (no MIBG scores, INRC responses, or tumor measurements)
- For ongoing cooperative trials
  - Outcome data are only available after publication of the main study results
- Metastatic site information for ~50% of COG patients
**INRG Data Dictionary: What's next?**

• Ongoing efforts to expand the data dictionary to include
  – Relapse Data (relapsed vs. refractory / time to next relapse / treatment assigned at 1st relapse/refractory trial)
  – Pre-clinical Data
  – Response Data
    – subsets will have uploaded MIBG scans (limited)
    – Baseline and post-induction Curie/SIOPEN score
  – Genomics
    – Some data linked to genomics datasets (eg TARGET)
    – Prioritizing biomarkers (INRG Genomics Com)
### INRG : Genomics 2021

#### Next steps

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<tr>
<th>MYCN</th>
<th>INTEGER</th>
<th>MYCN status</th>
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<tr>
<td></td>
<td></td>
<td>1=Amplified (&gt;4 times of the reference on chromosome 2q)</td>
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<tr>
<td></td>
<td></td>
<td>0=Not amplified (&lt; 4 times of the reference on chromosome 2q)</td>
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<td>9=Unknown, not done, unsatisfactory, in progress</td>
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<tr>
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<td>1=DNA Index ( \leq 1 ) (hypodiploid, diploid)</td>
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<td>0=DNA Index ( &gt; 1 ) (hyperdiploid)</td>
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- 9=Unknown, not done, unsatisfactory, in progress

**Ploidy**
- 1=DNA Index ≤1 (hypodiploid, diploid)
- 0=DNA Index > 1 (hyperdiploid)
- 9=Unknown

**Data Sources**
- SCAs, NCAs
- More loci
- SIOPEN 7
- ALK variant
- %, tumor, ctDNA

**INRG : Genomics 2021**

**future**

**more detailed data, inc. variables**

[September 22, 2021](https://inrgdb.org/)
How to frame your research

Mark Applebaum
How to start your proposal?

Lucas Moreno
How to start an INRG Project/ Application?

1. Idea
2. Contact us
3. Cohort Discovery
4. Application

You can also approach us if you are interested in participating or developing an INRG project but don't have a specific idea.

mentorship@inrgdb.org
http://inrgdb.org/get-involved/

https://inrgdb.org/
INRG Application Form

- Authors
- Statistician
- Project Proposal
  1. Specific Aims
  2. Hypothesis
  3. Patient Cohort (Eligibility Criteria)
  4. Background
  5. Significance
  6. Proposal description
  7. Data Requested
Statistician Resources

• All INRG database projects require statistician co-investigator/collaborator
  — Either collaborate with one of the INRG statistician committee members OR
  — Local statistician (at investigator’s university/institution) who must be approved by the INRG statistics committee
  — Resources may be available for new investigators (1st INRG project)

• How does the statistician help investigators with their analyses:
  — Study design
  — Feasibility
  — Statistical analyses
  — Familiarity with INRG database
Proposal Process

• Mentor input
  • Team up new investigator/YI with mentor familiar with INRG for project development and/or collaborations
  • mentorship@inrgdb.org

• Submission – review & approval process by INRG Executive
List of Potential Projects

Lucas Moreno
Potential Projects

- Re-analysis
- New Analyses
- Non-Data
Potential Projects - Re-analysis

- Clinical and biological features predictive of survival after relapse, in progress by several groups (London, J Clin Oncol 2011)

- The INRG classification system in progress by several groups [Irwin, Fischer, London], (Cohn, J Clin Oncol 2009)

- Prognostic significance of pattern and burden of metastatic disease in patients with stage 4 neuroblastoma (Morgenstern, Eur J Cancer 2016)

- Subgroup analysis
  - “Stage 3” – in progress by COG/SIOPEN, Meany, Pediatr Blood Cancer 2014
Potential Projects - New Analyses

• New genomic data in INRG
• New relapsed data in INRG
• New response data in INRG
• Impact of treatment modalities that can be “de-coded” from trial participation
• LCNRG risk classifier for patients at LMIC (Wendy London)
Potential Projects - Non-Data

• White papers and consensus documents
  • Ongoing white paper on NB Biology research (Meredith Irwin, Gudrun Schleiermacher, Matthias Fischer)

• Systematic reviews (ongoing by Lucas Moreno & Wendy London)
  • Prognostic biomarkers in high risk NB at diagnosis
  • Prognostic biomarkers in high risk NB in response to therapy
Q&A

Lieve Tytgat
Q&A

• Enter your name in the chat
• Enter your question in the chat
• Raise your hand
Closing remarks and next steps

Meredith, Lucas, Mark, Lieve, Wendy
Next

• Please submit your project ideas to mentorship@inrgdb.org
• A follow-up meeting will be planned to discuss project ideas in detail
• Thank you!
We gratefully acknowledge and thank

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See you in real life

- ANR 2022  08-12 May 2022 Amsterdam
- ANR 2024  China

- Thanks and stay safe