INRG

International Neuroblastoma Risk Group

TASK FORCE

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

Wednesday, September 22, 2021

US PDT	US CDT	US ET	BST	CEST	Length
08:00	10:00	11:00	16:00	17:00	1 hour

Welcome
Introduction

Meredith Irwin

-on behalf of INRG Strategy Development Committee

- https://inrgdb.org/get-involved/

Your hosts

Meredith Irwin	meredith.irwin@sickkids.ca
Lucas Moreno	lucas.moreno@vhebron.net
Mark Applebaum	mapplebaum@peds.bsd.uchicago.edu
Lieve Tytgat	g.a.m.tytgat@prinsesmaximacentrum.nl
Wendy London	Wendy.London@childrens.harvard.edu
Suzi Birz	suzi@uchicago.edu






Agenda

Welcome and Introductions	Meredith	5 minutes
Summary of existing projects	Meredith	5 minutes
Introduction to INRG data dictionary	Meredith	5 minutes
How to frame your research	Mark	20 minutes
How to start your proposal	Lucas	5 minutes
List of potential projects	Lucas	10 minutes
Q&A	Lieve	8 minutes
Closing remarks and next steps		2 minutes

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
  - https://inrgdb.org/wp-content/uploads/2019/09/Expanding-the-INRG-Community.pdf
  - 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

MYCN	INTEGER	MYCN status	1=Amplified (>4 times of the reference on chromosome 2q) 0=Not amplified (≤ 4 times of the reference on chromosome 2q) 9=Unknown, not done, unsatisfactory, in progress	
PLOIDY	INTEGER	Ploidy	1=DNA Index ≤1 (hypodiploid, diploid) 0=DNA Index > 1 (hyperdiploid) 9=Unknown	
DNA_INDEX	DECIMAL	DNA Index		
_11Q_UBAB	INTEGER	Either an 11q aberration or unbalanced 11q	0=No loss or no aberration 1=Deletion 9=Unknown, pending, cannot be determined	
_1P_LOAB	INTEGER	1p or 1p abberation	0=No loss or no aberration 1=Deletion 9=Unknown, pending, cannot be determined	
_17Q_GAIN	INTEGER	17q gain	0=No gain 1=Gain 9=Unknown, pending, cannot be determined	
ALK	INTEGER	ALK genomic status	0=No alteration 1=Mutation 2=Amplification 9=Unknown, pending, cannot be determined	

INRG : Genomics 2021 ➡ future

more detailed data, inc. variables

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➡ SCAs, NCAs
More loci
SIOPEN 7

➡ ALK variant %, tumor, ctDNA

How to frame your research

Mark Applebaum

How to start your proposal?

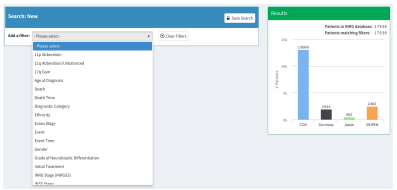
Lucas Moreno

How to start an INRG Project/ Application?

Idea → Contact us → Cohort Discovery → Application

mentorship@inrgdb.org

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



You can also approach us if you are interested in participating or developing an INRG project but don' have a specific idea

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
  - Localised/infant NB with MYCN amplification – Bagatell, J Clin Oncol 2009, Taggart J Clin Oncol 2011

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

St. Baldrick's FOUNDATION
Conquer Childhood Cancers

SAMMY'S SUPERHEROES FOUNDATION

WILLIAM GUY FORBECK RESEARCH FOUNDATION
wgfrf.org

Children's Neuroblastoma Cancer Foundation

The Neuroblastoma Children's Cancer Society

THE MATTHEW BITTKER FOUNDATION
It's What Matters

CHILDREN'S RESEARCH FOUNDATION
"So they may live"

The Super Jake Foundation

ANDREW McDONOUGH B+ FOUNDATION

LITTLE HEROES

AT THE FOREFRONT OF KIDS MEDICINE
UChicago Medicine Comer Children's
Development Board

Alex's Lemonade Stand
FOUNDATION FOR CHILDHOOD CANCER

Mr. Daniel Tierney

US Department of the Interior

NIH NATIONAL CANCER INSTITUTE

See you in real life

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

- Thanks and stay safe