



**PRADER WILLI RESEARCH
FOUNDATION AUSTRALIA**

Current PWS Research

Kathleen Jones, CEO & Founder

Dr Diane Webster, Research Director



Skyla, 2



Tom, 7



Mitchell, 9



Olivia, 11

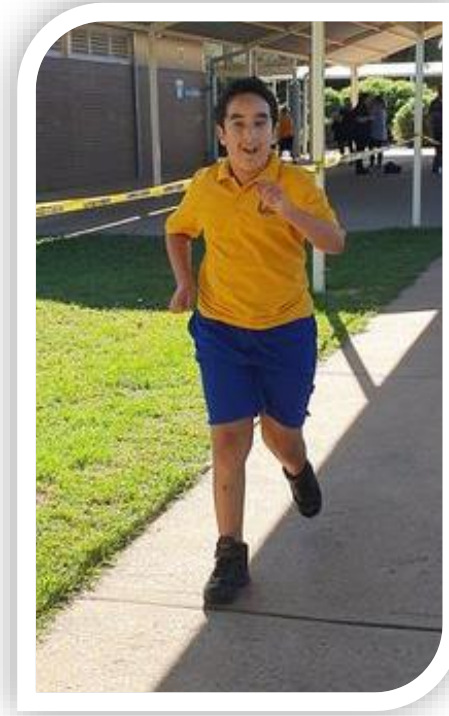
Diane's video here

Slide formatting to
match slide 2

Dr Diane Webster, *Research Director*

Prader Willi Research Foundation Australia

Our vision is to improve clinical outcomes and deliver better treatments for people living with PWS



Prader Willi Research Foundation Australia

Strategic research focus:

- gene activation by epigenetic editing
 - therapies targeting the underlying cause of PWS
- new therapies for the most important symptoms
 - Basic science to clinical trials
- Infrastructure
 - to support all stages of therapy development
- delivering better healthcare



Kath – video of you will go in this box


PWS research themes

Capturing PWS lived experience

- patient voice
- caregiver burden
- therapy choices (risk tolerance)
- consensus definitions

Original Research Article

MDMP&P
Policy & Practice

MDM Policy & Practice
1-9
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Measuring Meaningful Benefit-Risk Tradeoffs to Promote Patient-Focused Drug Development in Prader-Willi Syndrome: A Discrete-Choice Experiment


Jui-Hua Tsai*, Norah L. Crossnohere*, Theresa Strong, and John F. P. Bridges

REVIEW

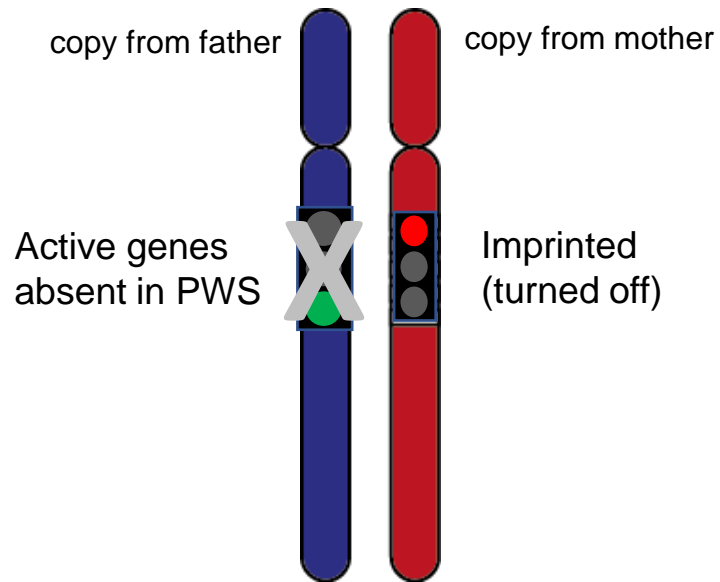
Open Access

Behavioral features in Prader-Willi syndrome (PWS): consensus paper from the International PWS Clinical Trial Consortium

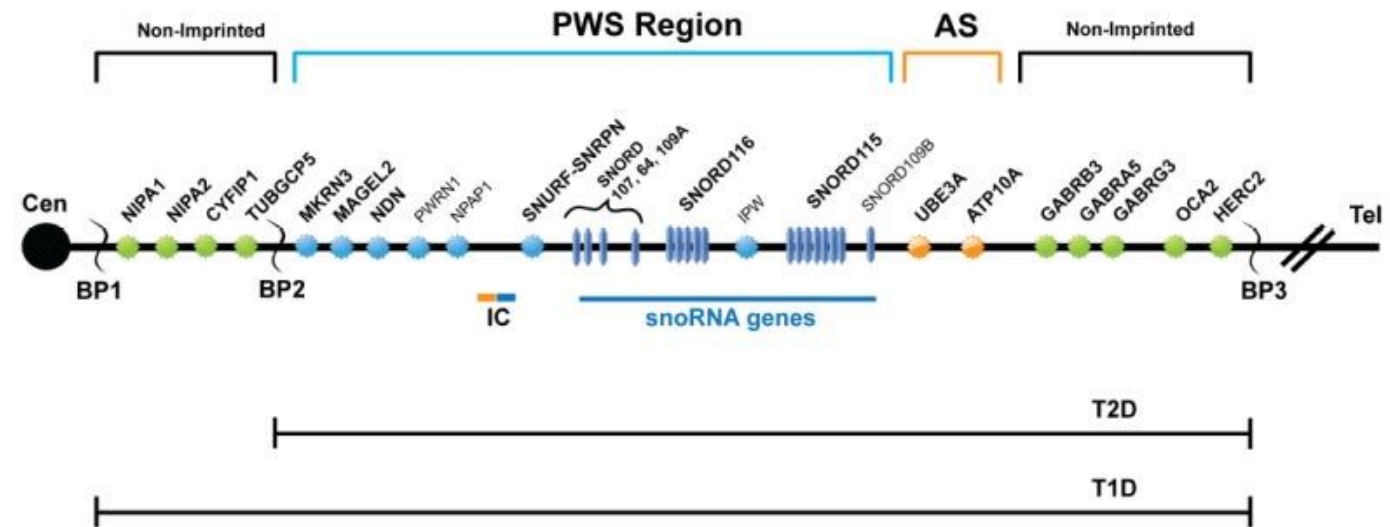


Lauren Schwartz^{1,2*}, Assumpta Caixàs^{3,4}, Anastasia Dimitropoulos⁵, Elisabeth Dykens⁶, Jessica Duis⁷, Stewart Einfeld⁸, Louise Gallagher⁹, Anthony Holland¹⁰, Lauren Rice¹¹, Elizabeth Roof¹², Parisa Salehi¹³, Theresa Strong^{1,14}, Bonnie Taylor¹⁵ and Kate Woodcock¹⁶

Research theme: behind the scenes



Chromosome 15



Driscoll et al. Gene Reviews 2017



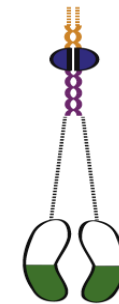
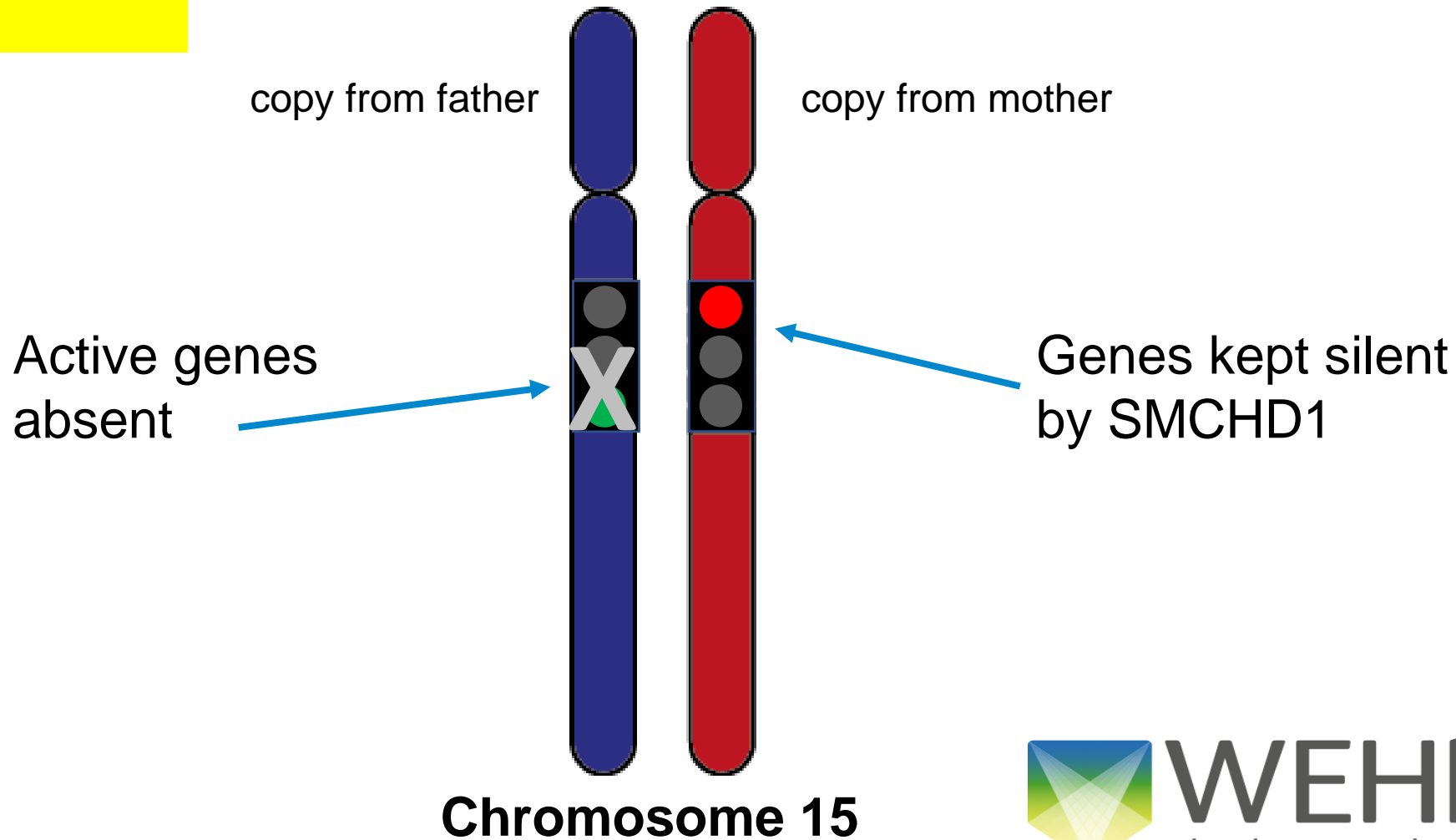
***Smchd1* is a maternal effect gene required for genomic imprinting**

Iromi Wanigasuriya^{1,2†}, Quentin Gouil^{1,2†}, Sarah A Kinkel^{1,2}, Andrés Tapia del Fierro^{1,2}, Tamara Beck¹, Ellise A Roper³, Kelsey Breslin¹, Jessica Stringer⁴, Karla Hutt⁴, Heather J Lee³, Andrew Keniry^{1,2}, Matthew E Ritchie^{1,2,5}, Marnie E Blewitt^{1,2*}

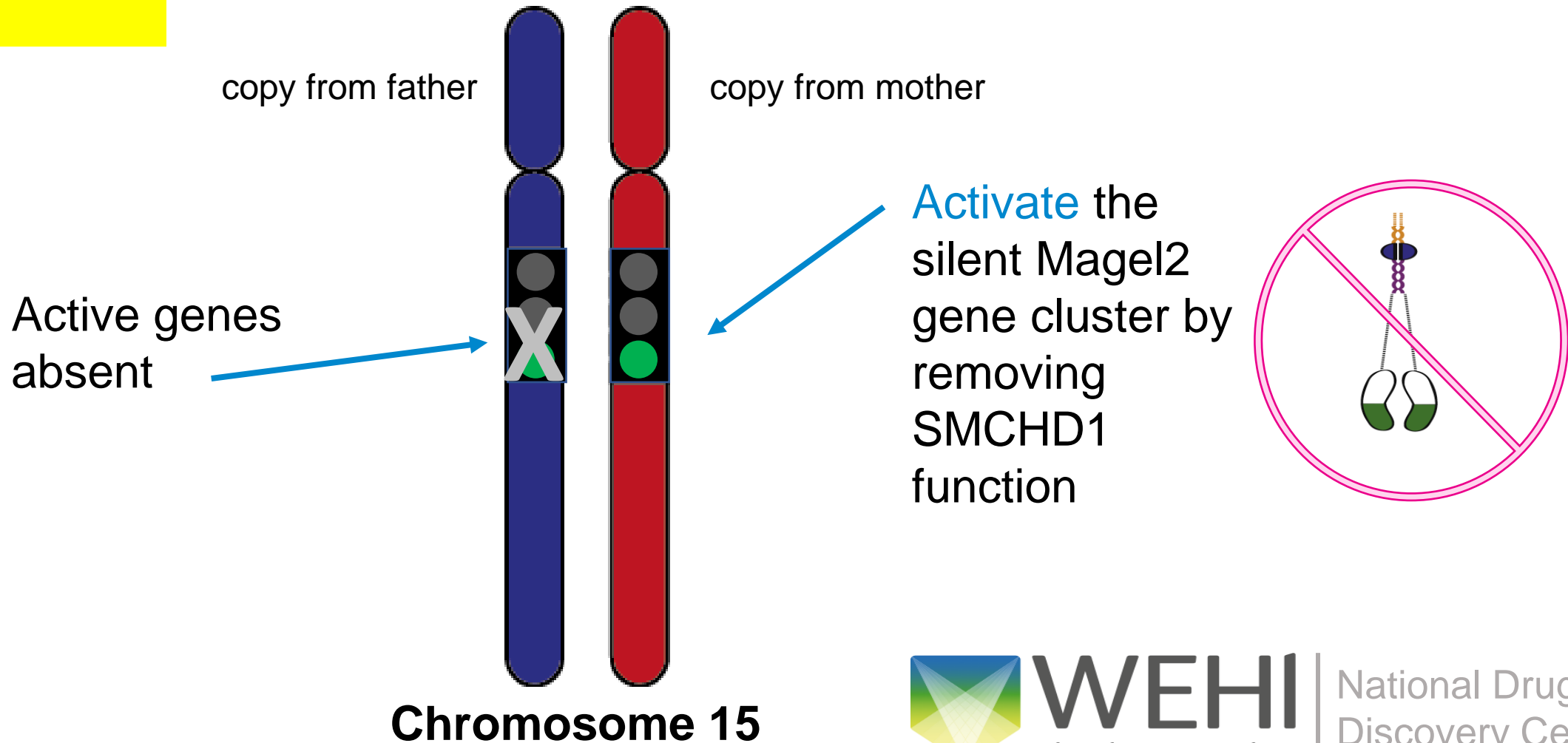
¹Walter and Eliza Hall Institute of Medical Research, Parkville, Australia; ²The Department of Medical Biology, The University of Melbourne, Parkville, Australia; ³Faculty of Health and Medicine, The University of Newcastle, Newcastle, Australia; ⁴Monash Biomedicine Discovery institute, Monash University, Clayton, Australia; ⁵The Department of Mathematics and Statistics, The University of Melbourne, Parkville, Australia

Abstract Genomic imprinting establishes parental allele-biased expression of a suite of mammalian genes based on parent-of-origin specific epigenetic marks. These marks are under the control of maternal effect proteins supplied in the oocyte. Here we report epigenetic repressor *Smchd1* as a novel maternal effect gene that regulates the imprinted expression of ten genes in mice. We also found zygotic SMCHD1 had a dose-dependent effect on the imprinted expression of seven genes. Together, zygotic and maternal SMCHD1 regulate three classic imprinted clusters and eight other genes, including non-canonical imprinted genes. Interestingly, the loss of maternal

Treating the cause of PWS



Treating the cause of PWS



Identifying SMCHD1 inhibitors

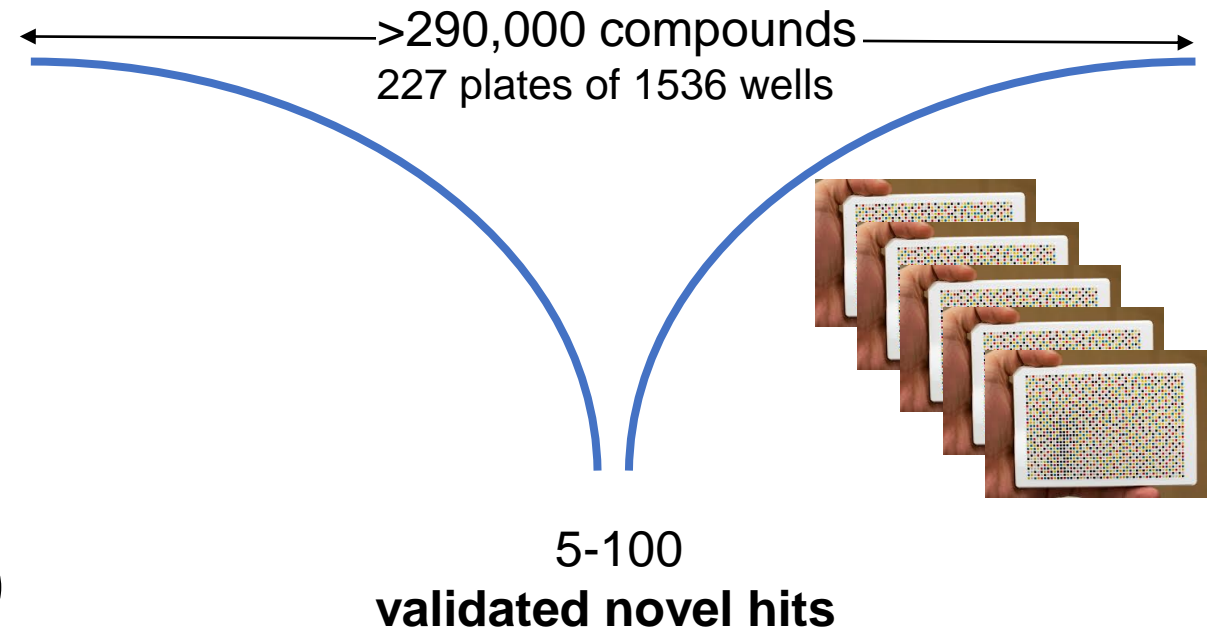
High throughput chemical screens

- >2500 hits

Validation

- Replicate the findings in the same assay
- Test to ensure they don't inhibit the assay
- Replicate in a different assay

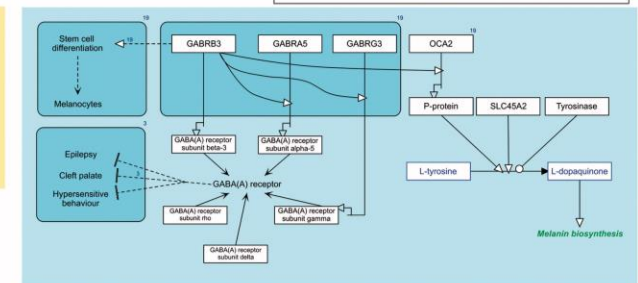
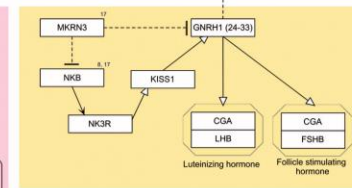
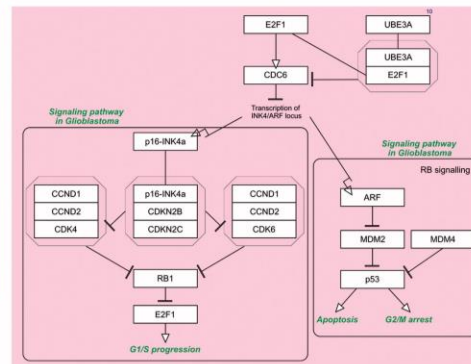
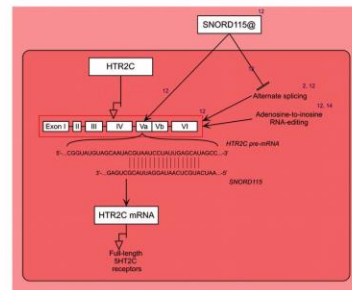
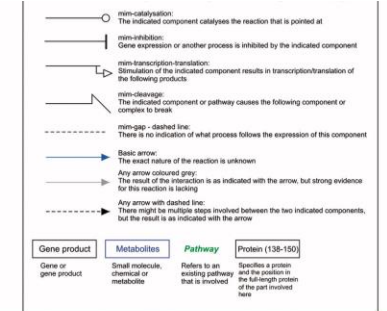
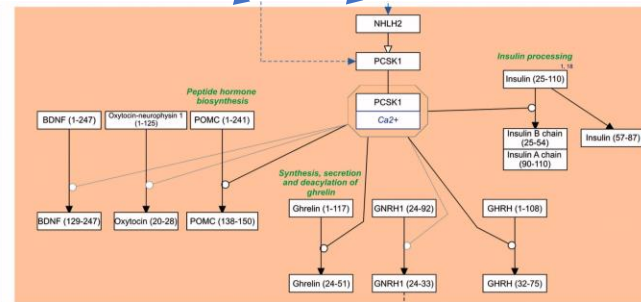
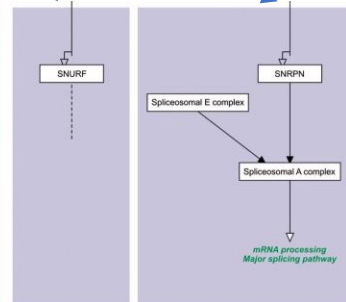
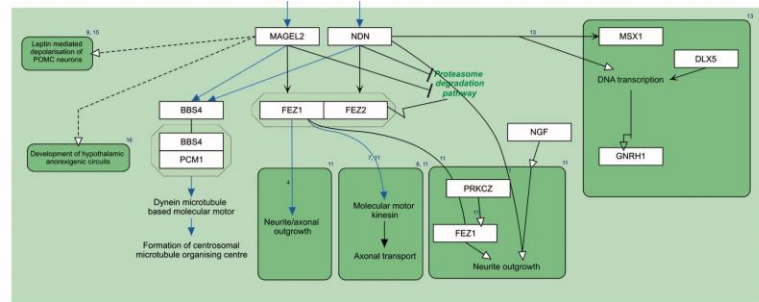
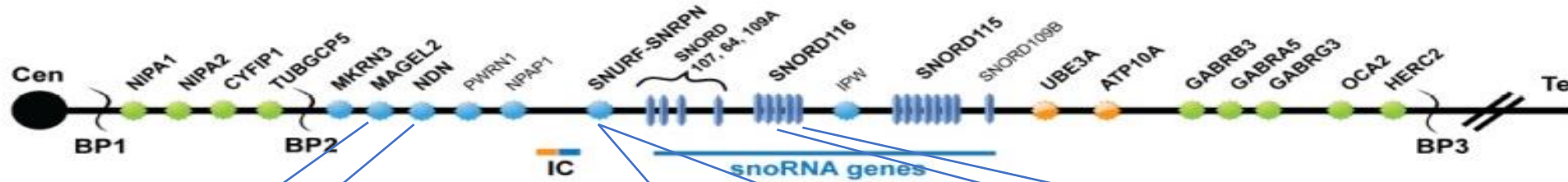
Lead molecule selection (5-6 compounds)



WEHI
brighter together

National Drug
Discovery Centre

Behind the Scenes – digging deeper



Clinical studies

Clinical Trials

- Intranasal Carbetocin (LV-101/Levo Therapeutics)
- DCCR (Solenio Therapeutics)
- Microbiome
- Growth hormone

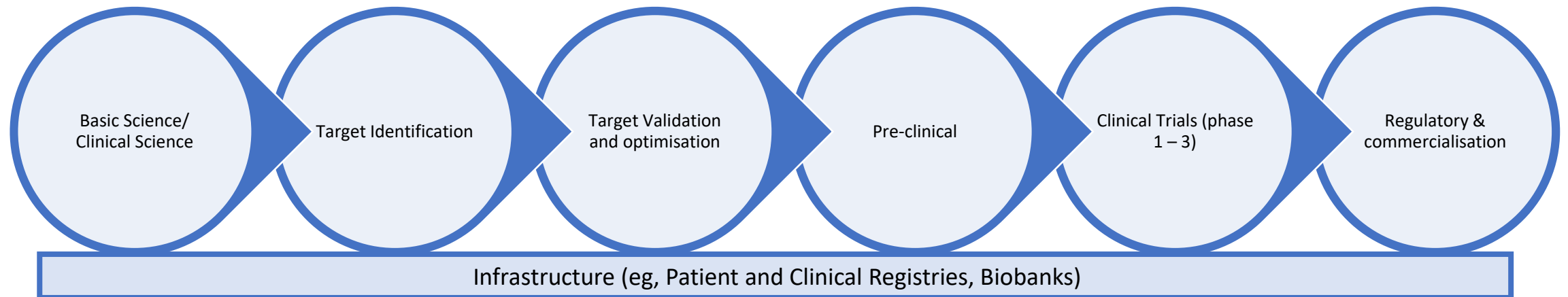
- Many other studies are underway

Clinical Observations and Biomarkers

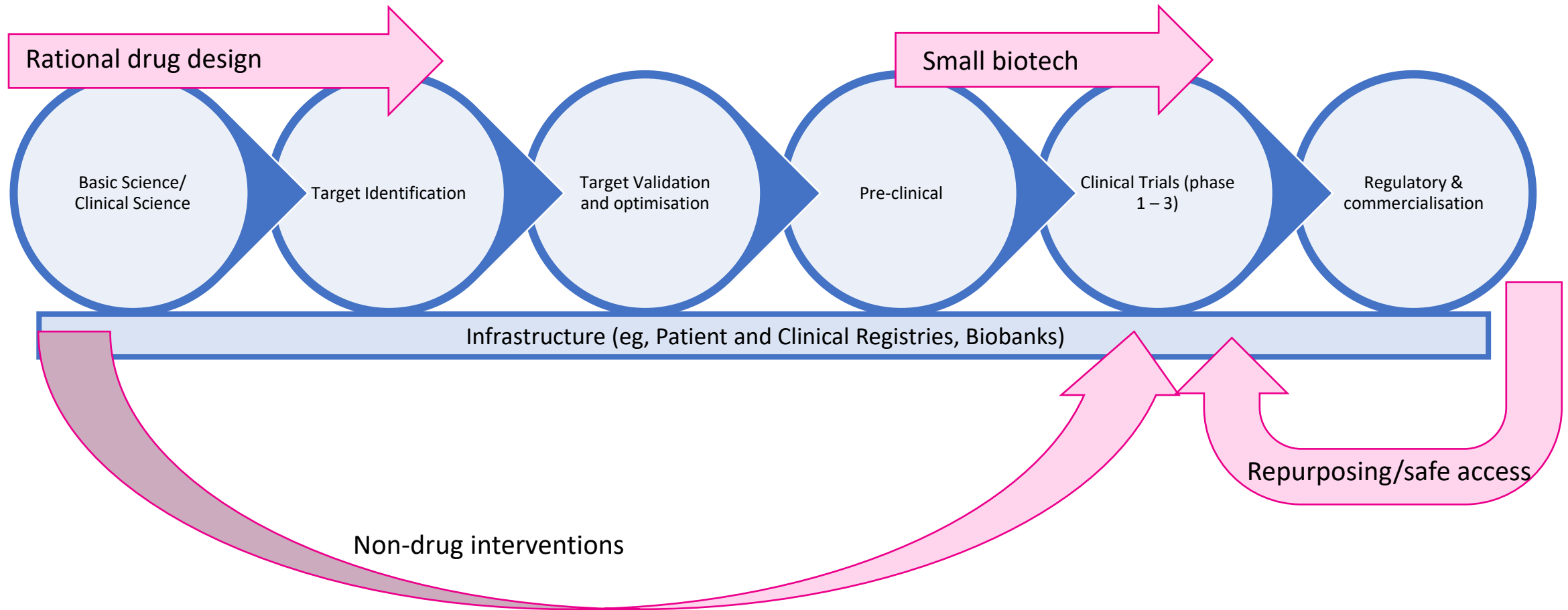
- tools for understanding what's happening at a clinical level
- new therapeutic targets, opportunities, learnings

Sleep, exercise, COVID, meta-analysis... and more...

Developing PWS therapies

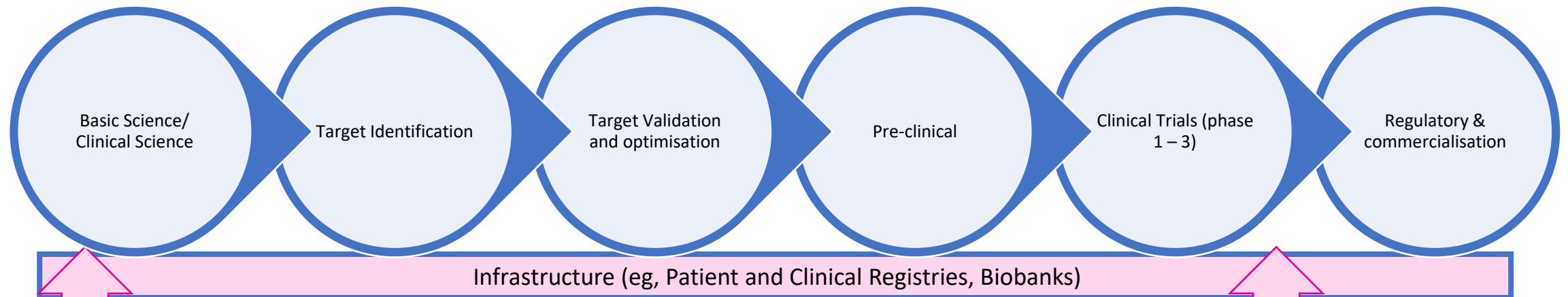


Developing PWS therapies



Supporting research

Nothing about me – without me! Advocacy has a role at every stage. Share your stories



Fundraising to support
research

Join a registry and/or biobank

Enroll in clinical trials that
are right for you

Chromosome 15 Biobank



The Biobank will collect and store

- Biological samples
- Clinical histories and detailed-phenotypic data

The objective of the biobank is to enhance PWS and AS research and clinical practice by:

- Making data and biological specimens available to other researchers and industry, to answer key questions
- Fostering collaboration between academics and industry
- Maximising the impact of laboratory and clinical assessments and data linkage for people with PWS and their families
- **Efficiency is the Moto: 'collect once and share – rather than 100 times and don't'**

For more information please contact emma.baker@mcri.edu.au



Laurence G & Jean E
Brown Charitable Trust

Prader Willi Research Foundation Australia

"This artwork was created by children with PWS who look forward to the day better treatments exist"



Skyla, 2



Tom, 7



Mitchell, 9



Olivia, 11

We'd love to hear from you

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- diane.webster@praderwilli.org.au