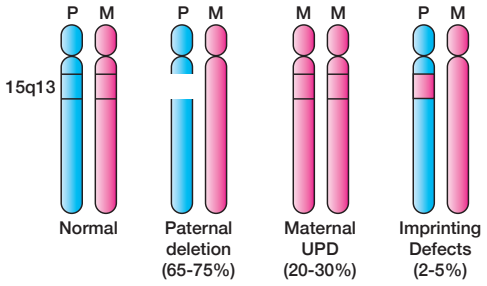
Walter+Eliza Hall Institute of Medical Research
DISCOVERIES FOR HUMANITY

Silencing SMCHD1 to treat Prader-Willi Syndrome (PWS)

- **There is currently no treatment targeting the genetic cause of PWS available**
- **We showed that Smchd1 deletion in committed cells causes selective gene reactivation at the PWS cluster**
- **Seeking partners to progress the development of SMCHD1 inhibitors as a potential PWS therapy**

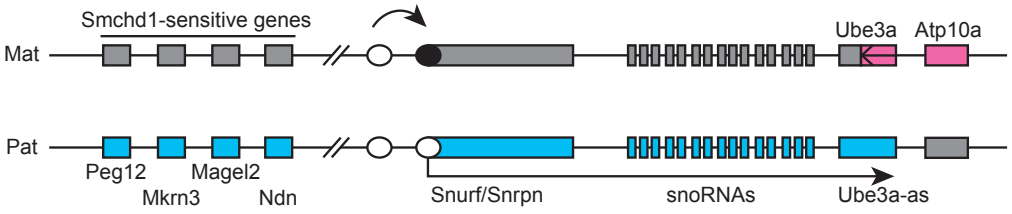
The opportunity

PWS occurs due to mutations in the paternal allele causing a failure to express critical genes. It affects 1 in 10,000 newborns and medical care per patient is between $30-66K annually. Current treatments target symptoms instead of the genetic cause of PWS.



The technology

SMCHD1 represses PWS critical genes on the maternal allele.



We showed selective gene reactivation from Smchd1 deletion, suggesting that SMCHD1 could be a potential PWS therapy target (Table 1).

Table 1: Selective gene reactivation from Smchd1 deletion

Smchd1 binding sites	Embryos	Committed cell (maternal allele)
Hox clusters	Failed silencing	Silencing maintained
X Chromosome	Failed silencing	Silencing maintained
PWS cluster	Failed silencing	Gene reactivated

Opportunities for partnership

We are seeking partners to co-develop SMCHD1 inhibitors.

We have:

- Foremost experts in SMCHD1, a world class structural biology program and an excellent understanding of SMCHD1
- A SMCHD1 inhibitor and in vitro neural cell assays to conduct initial testing

We are seeking investments to:

- enable the *in vivo* validation of Smchd1 inhibition in PWS mouse model
- perform proof-of-concet experiments in patient iPSC-derived hypothalamic neurons
- complete our medicinal chemistry program

Scientific team

Associate Professor Marnie Blewitt
Division Head, Molecular Medicine Division

Associate Professor James Murphy
Laboratory Head, Cell Signalling and Cell Death Division

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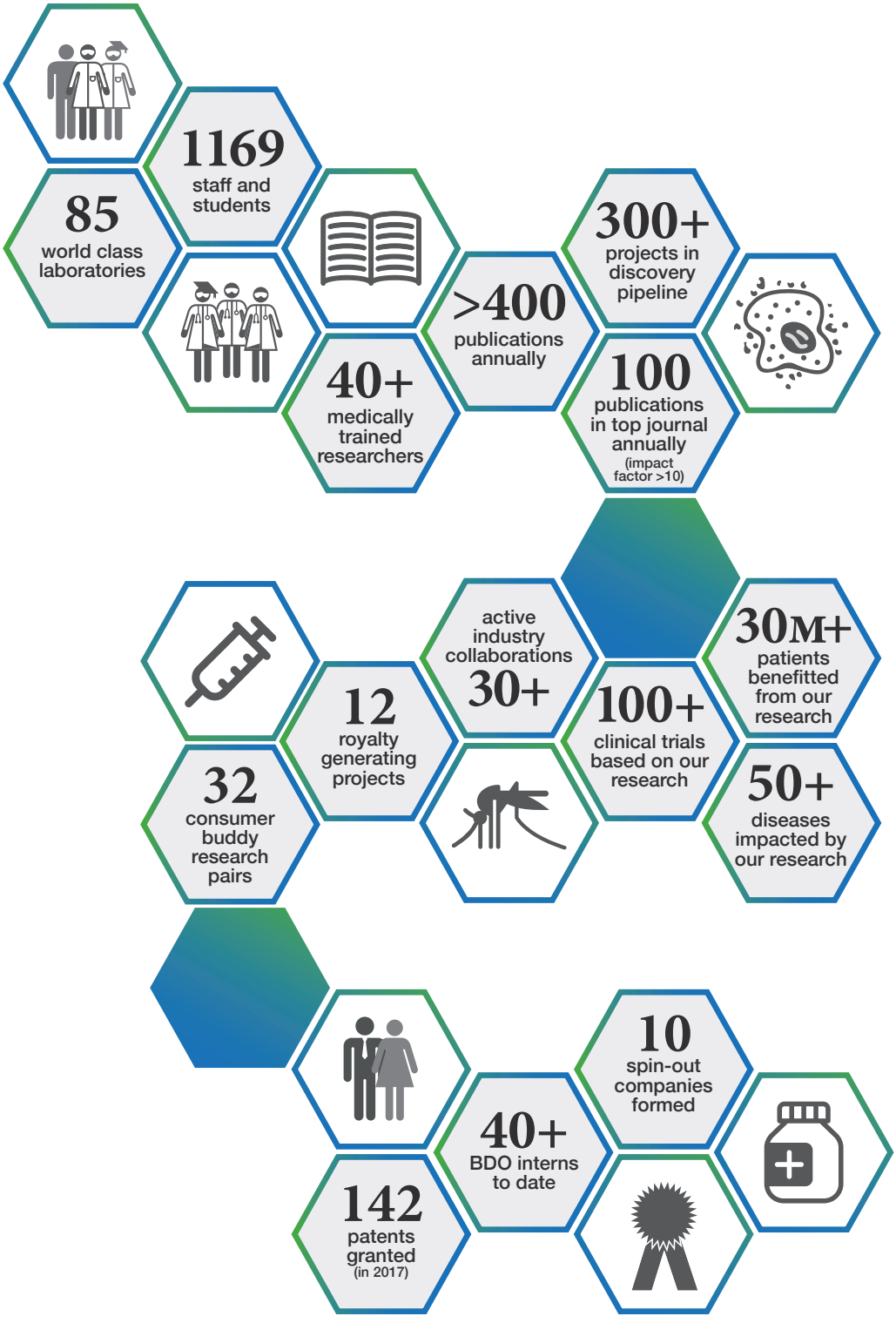
Walter and Eliza Hall Institute of Medical Research

At the Walter and Eliza Hall Institute our multidisciplinary research teams are focused on solving complex biological questions by integrating expertise in bioinformatics, clinical translation, computational biology, epidemiology, genomics, medicinal chemistry, proteomics, structural biology and systems biology. Our innovative science expands and improves the understanding of human biology and enables the translation of this new knowledge into novel therapies that benefit patients worldwide.



To discuss partnering opportunities, please contact **Dr Anne-Laure Puaux**, Head of Commercialisation, by email **puaux.a@wehi.edu.au** or phone +61 3 9345 2175.