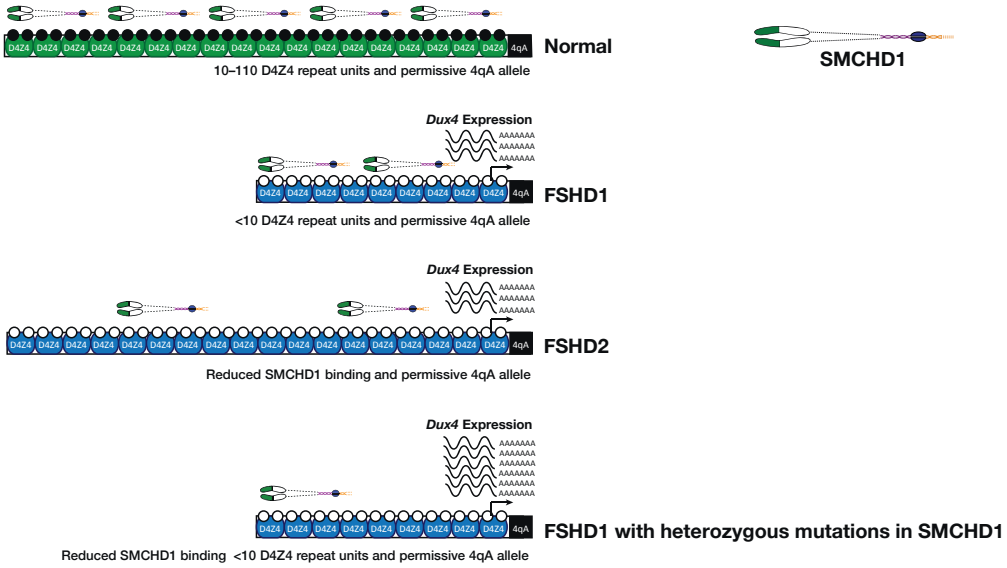
Walter+Eliza Hall Institute of Medical Research
DISCOVERIES FOR HUMANITY

Activating SMCHD1 to treat facioscapulohumeral muscular dystrophy (FSHD)

- **There is currently no specific treatment available for FSHD, a genetic muscle disorder caused by abnormal expression in adult cells of the transcription factor DUX4.**
- **SMCHD1 is an important repressor of DUX4 that possesses enzymatic (ATPase) activity; altered ATPase activity of SMCHD1 has been shown in disease.**
- **Activation of SMCHD1 is a potential FSHD therapy.**

The opportunity

FSHD is a genetic muscle disorder mostly affecting muscles of the face, shoulder blades and upper arms. It is estimated to affect about one in 7500 to one in 20,000 individuals worldwide. FSHD is caused by expression in adult cells of the transcription factor DUX4, which is normally silenced following embryonic development by SMCHD1 and other epigenetic repressors.



The technology

We have shown that SMCHD1 contains a GHKL-ATPase domain and confirmed that it possesses enzymatic activity. Decreased ATPase activity has been found in FSHD patients suggesting that activation of SMCHD1 activity could be a potential FSHD therapy.

Opportunities for partnership

We are seeking a partner to co-develop SMCHD1 activators for FSHD therapy.

We have:

- Foremost experts in SMCHD1, a world-class structural biology program and an understanding of SMCHD1 structure.
- High quality recombinant protein, validated screening assays and capability for structure-guided medicinal chemistry.

We are seeking a partner:

- To invest in our medicinal chemistry program to follow up identified hits from an ongoing fragment-based drug discovery campaign.
- With culture systems of human muscle cell systems to validate activator hits.

Scientific team

Associate Professor Marnie Blewitt
Division head, Epigenetics and Development division

Associate Professor James Murphy
Division head, Inflammation division

Partnering opportunities

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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.

Project pipeline - available for partnering

	Project	Mode of action*	Target validation	Hit discovery	Lead generation	Lead optimisation	Indication
Cancer	Targeting minor class splicing	Inhibitor					Mutant K-Ras, B-Raf tumours
	Targeting EBV malignancies	Inhibitor					Burkitt's lymphoma
	Treating drug resistant cancers	Inhibitor					Cancer
Immune health and infection	pDC therapy for lupus	Inhibitor					Systemic lupus erythematosus
	RIPK2: Intercepting Inflammation	Inhibitor					Inflammatory bowel disease
	Rethinking CD52	Biologic					Autoimmunity
	SOCS mimetic	Inhibitor					Inflammatory bowel disease
	A complete cure for HBV	Inhibitor					Hepatitis B
	Novel malaria vaccine	Vaccine					Malaria
	Toxoplasma vaccine	Vaccine					Animal health: Toxoplasmosis
	Precision prebiotics	Prebiotic					Inflammation
Healthy development and ageing	Precision epigenetics	Inhibitor					Prader-Willi Syndrome
	FSHD epigenetic therapy	Activator					Facioscapulohumeral dystrophy
	Improving retinal detachment outcomes	Inhibitor					Ophthalmology

*Activator or Inhibitor refers to small molecule compounds

To discuss partnering opportunities, please contact **Dr Anne-Laure Puaux**, Head of Commercialisation, by email **partnering@wehi.edu.au**.