

Structure of protein pair provides blueprint for future drugs

June 1 2018



Structural biology researchers (from left) Dr Nick Liao, Associate Professor Jeff Babon and Dr Nadia Kershaw have revealed the structure of revealed how the SOCS1 protein switches off cell signaling. Credit: Walter and Eliza Hall Institute of Medical Research

Walter and Eliza Hall Institute researchers have visualised for the first time how the protein SOCS1 'switches off' cell signalling to dampen immune responses and block cancer growth.

The atomic-level structure of SOCS1 binding to its partner [protein](#) JAK could guide the development of drugs that alter disease-causing cell signalling pathways, and may have applications for treating some blood cancers, including leukaemias.

The research, led by Dr. Nick Liao, Dr. Nadia Kershaw, Associate Professor Jeff Babon and Professor Nick Nicola, was published in the journal *Nature Communications*.

Switching off signalling

Dr. Liao said the structure of the protein pair revealed for the first time how SOCS1 binds to JAK proteins to disable signalling.

"Using the Australian Synchrotron and the CSIRO Collaborative Crystallisation Centre, we produced an incredibly detailed view of how SOCS1 interacts with the JAK1 protein," Dr. Liao said. "With this image, we were able to explain for the first time why JAK proteins cannot signal when bound to SOCS1. This information could help to underpin the development of new medicine targeting this important cell signalling pathway."

A blueprint for new medicines

Dr. Kershaw said both SOCS1 and JAK proteins had been implicated in driving diseases including cancer and inflammatory conditions.

"In particular, overactive JAK signalling is linked to the development of cancer-like conditions called myeloproliferative neoplasms (MPNs) – which include polycythemia vera, essential thrombocythemia and primary myelofibrosis – as well as certain acute childhood leukaemias.

"Medicines that inhibit JAK signalling are in use for treating MPNs, but they are only able to manage the disease, not cure it. New medicines for these conditions are needed, and we envisage that a drug designed to mimic the SOCS1 protein to switch off JAK proteins might be a more effective treatment," Dr. Kershaw said.

As well as guiding the development of drugs mimicking SOCS1, the team's research may also underpin the development of a second new class of drugs that inhibit SOCS1, Associate Professor Jeff Babon said. "SOCS1 binding JAK proteins normally applies a 'brake' to immune responses – which in a healthy person is a good thing," he said.

"However, in certain conditions, releasing this brake could be the key to enhanced immune responses. This approach to boosting the [immune response](#) could be the key to improving immunotherapies for treating cancer. If we could design a drug that inhibits SOCS1, this might boost anti-cancer immune responses, potentially improving anti-cancer immunotherapies."

More information: Nicholas P. D. Liao et al. The molecular basis of JAK/STAT inhibition by SOCS1, *Nature Communications* (2018). [DOI: 10.1038/s41467-018-04013-1](https://doi.org/10.1038/s41467-018-04013-1)

Provided by Walter and Eliza Hall Institute of Medical Research

Citation: Structure of protein pair provides blueprint for future drugs (2018, June 1) retrieved 17 July 2024 from <https://medicalxpress.com/news/2018-06-protein-pair-blueprint-future-drugs.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--