Towards targeted treatments for Fanconi Anaemia

Dr Wayne Crismani

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Dr Wayne Crismani from the St Vincent's Institute (SVI) of Medical Research is undertaking research focussed on dissecting the molecular biology of an inherited Bone Marrow Failure Syndrome and cancer predisposing condition called Fanconi Anaemia. In the 1990s, the life expectancy of a patient with Fanconi Anaemia was horrifically less than 10 years of age. Thankfully, with advances in all fields of science, the current life expectancy of an individual with Fanconi Anaemia has improved and is approximately 35 years, but this statistic is still appalling. Dr Crismani emphasises, "There is no cure for Fanconi Anaemia, nor are there targeted treatments that address the root cause of the condition. The scientific gains have come from flow on effects in other fields. We investigate the fundamental biology of what goes wrong in Fanconi Anaemia and we are working towards translating this fundamental knowledge to effective treatments and early detection."

The SVI laboratory is made up of diverse people, generally in their 20s or 30s, with a range of skills - biochemists, biologists, data scientists and a nurse. It requires great expertise to work in a high standard of molecular biology today and collaborations are imperative, both nationally and internationally. Dr Crismani's team has a number of projects underway that include drug development, genetic studies with individuals with FA, early detection of cancer and fertility studies. While these projects may seem diverse, they all stem from the root cause of Fanconi Anaemia which is what is referred to as "genomic instability". Dr Crismani's team use multi-disciplinary approaches with a variety of methods including biochemistry, cell culture, mouse models, whole genome sequencing and epidemiology.

The research covers a number of stages in the research pipeline, "We ask many fundamental scientific questions, but we also have projects that are clinical and can result in the early detection of a cancer. There is a lot that needs to be done. Some areas that I see a need for include early and accurate detection of genetic conditions. A lot of genetic testing is currently being performed, but more investment is required in the laboratories that can provide validation of the results and the predictions that come out of these reports. I also feel that we are now in a position to develop targeted treatments including specific pharmaceutical products and also gene therapy. Gene editing with CRISPR/Cas9 technology is the discovery of a generation for molecular biologists. It offers the realistic chance of altering

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genetic mutations that cause disease to alleviate or prevent serious health conditions. These are just a few examples. It is extremely important that more money is directed towards basic and applied research."

Dr Crismani wishes to make a meaningful difference. "I think that the area that I am in makes the best use of my skills, and those of my team, to help individuals who truly need it. Our research will lead to early and accurate detection of serious health conditions. I do not want to give false hope as the roads to cures are long and very challenging. But we work hard towards creating transformative treatments for people affected by conditions such as Fanconi Anaemia."

One of the major barriers to researchers according to Dr Crismani is the severe lack of available funding. "The current prospects for a bone marrow failure researcher, and all academic scientists, is that their contracts are short, and their futures are uncertain. It is understandably tempting to leave for greener pastures in a completely different area of society where they can have a stable job, have a family and a mortgage. The answer seems so simple: put more money into research. In reality this is very hard to achieve but a number of countries do this simply by pledging a far superior amount of their gross domestic product to research. Unfortunately, Australia is below average for OECD countries and investment in science."

Dr Crismani is originally from Adelaide and attended university in South Australia. He has lived in a number of countries for his scientific career and spends most of his free time with his young family, enjoying traveling locally and abroad whenever possible. Dr Crismani has been extraordinarily generous devoting energy and time to Maddie's Vision; he is a current member of the 2021 National Symposium Steering Committee, and has recently taken on the role of chairing the Gene and Cellular Therapies Subcommittee. He has also been instrumental in securing funding from the US based Fanconi Anaemia Research Foundation to assist with establishing Fanconi Anaemia Support Australasia, a membership-driven volunteer organisation which aims to unite and inform the FA community in Australia and New Zealand.