The current recipient of the WG Norman Trauma Fellowship, Plastic Surgery Trainee Dr Alexander Cameron, has spent the past year researching the role of the oddly-named actin remodelling protein known as Flightless in the formation of hypertrophic scarring.

Discovered only a decade ago, the protein was named Flightless after its gene was mapped in the Drosophila, with scientists later finding that if one copy was knocked out, the insect had defective flight muscles.

Now also known as Flii, the protein has been found to be one of the players in what Dr Cameron described as “the tightly orchestrated interplay” of agents which lead to excessive scarring.

Comparing human skin samples and using animal models, Dr Cameron has found that Flii is increased after injury and remains elevated in scar tissue and that decreasing Flii results in improved scarring.

“Hypertrophic scarring results from an aberration of the normal wound healing process in which the inflammatory stage of wound healing is upregulated and prolonged resulting in over production of collagenous extracellular matrix by fibroblasts,” he said.

“This carries a large burden of disease and requires years of ongoing therapy and revision surgery because such patients suffer severe disfigurement while contracture can cause severe disability.

“Until now, TGF-, a pro-scarring cytokine, has been the most widely-studied agent affecting wound healing. Our research has shown that, among other functions, Flii is an upstream regulator of TGF- which means that if we can find a way to interrupt Flii’s action we could potentially improve wound healing and reduce scarring.

“Already we have developed an antibody to block the action of Flii which has just been trialled in preclinical animal models including pigs, while safety studies for human trials are imminent.

“Although wound healing is a very complex process and it is difficult to target one agent among many to make a major difference, we think that an anti-Flii treatment, in the form of an injection, cream or as part of a dermal matrix, could be one of a range of treatments developed in the next decade.”

Dr Cameron has been conducting his work as a member of Professor Allison Cowins’ Wound Healing Team at the Women’s and Children’s Health Institute in Adelaide as part of his PhD being undertaken under the supervision of Professor Cowin and Associate Professor Peter Anderson.
He described the research as greatly rewarding and said that if the work was successful, the anti-Flii treatment could theoretically be applied to a range of scarring-related pathologies.

Along with the WG Norman Trauma Fellowship given to Dr Cameron in both 2011 and 2012, he has also received the RACS Plastic Surgery Research Award for 2012, first prize in the Adelaide University Health Faculty Research Conference and the 2011 Don Robinson prize for best research by a Plastic Surgery Trainee in South Australia.

“I feel very lucky to be involved in this project because a lot of research can be years and years away from practical results whereas the results of this work are tangible,” Dr Cameron said.

“I am also the only clinician in the wound healing team and it is a great privilege to work with a team of highly skilled and motivated scientists. It is also a privilege to be supported financially by the College to undertake the research on a full time basis. I originally tried to combine the project with full time clinical work, but it was not feasible.

“I think surgeons benefit from a dialogue with scientists because at times the two professions can be working on a solution to the same problem, but in parallel, unaware of each other’s progress. I think it is vital for new developments that we work to break down the cultural barriers that divide us.”

This year, Dr Cameron will be visiting the US to collaborate with Professor Geoffrey Gurtner, a world leader in the field of scarring and a Plastic Surgeon at Stanford University and will also attend the International Burns Symposium to be held in Edinburgh.

He said he was looking forward to working with surgeon scientists in this major international facility and hoped to bring back skills to bridge the divide between the two.

“Professor Gurtner has been working on an animal model of scarring based on wound tension, so we are going to collaborate on the role that Flightless may play in regulating the response to mechanical tension at the cellular level,” Dr Cameron said.

“Hopefully in the future there will be more cross pollination between surgery and science because it is difficult for scientists working on a solution to a clinical problem to have the same experience and perspective as surgeons, who in this case are treating wounds and hypertrophic scars on a daily basis. Likewise, it is difficult for surgeons to keep abreast of progress in basic science or have the time to devote to animal and lab work.”

Dr Cameron is in the process of writing up his research to submit to the Journal of Clinical Investigation and aims to present his work while in the US.

The WG Norman Research Fellowship arose from a bequest from the late WG Norman of Adelaide. The South Australian award was established to fund advances in surgery on injuries occasioned by any form of accident or trauma to young persons. Subsequently, the fellowship was broadened to encompass any research with a trauma focus.

With Karen Murphy