The genetics of healthy ageing and cancer

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We're living longer. That means that we're all at greater risk of cancer and we'll all suffer from bone loss. And for many of us, our final years will be difficult.

Josef Penninger plans to change all that. His vision is of a future where we can safely surf and live active lives at 85 years of age without fear of fracture, cancer or any of the other scourges of ageing. He's director of Austria's Institute of Molecular Biotechnology, and is in Australia as a guest of the Centenary Institute in Sydney to share his vision for a healthy old age, and discuss the research that's getting us there.

More than a decade ago Professor Penninger proved that a protein called RANKL is the master regulator of bone loss. That work led to a new drug now used for treating osteoporosis and skeletal related events associated with cancer.

He then showed that the same protein is involved in sex hormone driven lactation in pregnancy.

He later showed that RANKL is a key driver of breast cancer initiation in response to sex hormones, thus providing a molecular connection between hormone replacement therapies, the Pill, and breast cancer.

In his latest work he's identified a molecular brake that can turn on so called natural killer cells, a component of the immune system.
"Our immune systems are built to see and respond to danger," he says.

"Inflammation is a key response. But as we get older the immune system's own inflammatory response starts to cause problems. At the same time the immune system struggles to recognise cancer and respond."

Last month, he and his colleagues reported in *Nature* that a molecule called Cbl-b stops natural killer cells from recognising and killing cancer cells. By turning that molecule off, his laboratory showed that the killer cells could get on with their job and markedly reduce the spread or metastasis of cancer cells.

All of this work is in mice, but bodes well for a new generation of drugs to help our immune systems better cope with the challenges of ageing, and for a future in which we age healthily then die without years of chronic disease.

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