BAD gene HUNTING

A pioneering study into high cholesterol levels among Barossans of Silesian descent hopes to blunt the impact of the so-called 'German gene' and save hundreds of people from suffering heart attacks and premature death.

WORDS **NIGEL HOPKINS**

When Pastor August Kavel arrived at Port Adelaide in November 1838, bringing with him 250 people fleeing religious persecution in Prussia, he also brought with him a rogue gene that would, over the next 175 years, lead to the premature deaths of hundreds, if not thousands, of their descendants.

It's what Professor Ian Hamilton-Craig, an academic cardiologist, calls "the German gene" and there's no way the august Pastor Kavel, nor any of his intrepid followers, could have known a thing about it.

The fact that so many people would die prematurely from heart attack is unlikely to have caused much alarm at a time when long life was such a rarity – and so many other things could, and did, kill you.

But for Queensland-based cardiologist Prof Hamilton-Craig, all his years of experience in cholesterol research in Australia and overseas were sending him a very clear message.

For many years Prof. Hamilton-Craig practised in North Adelaide, where he had a significant number of patients from the Barossa. He recognised that many people of German descent had genetic high cholesterol – known as familial hypercholesterolaemia (FH) – which results in high cholesterol and an increased risk of premature coronary heart disease (CHD).

The errant gene at the centre of this problem is called FH Morocco because it was first identified in the Moroccan population, quite independently of any German influence.

Now Prof. Hamilton-Craig, who is based at the Centre for Preventative Cardiology and Internal Medicine at Griffith University on the Gold Coast, has initiated the Barossa Family Heart Study, in conjunction with genetics expert Professor Frank van Bockxmeer, from the University of Western Australia

The study is designed to locate residents in the Barossa Valley of Silesian descent who may have inherited the FH Morocco gene which causes very high cholesterol levels and possible premature heart attack and sudden coronary death.

Prof Hamilton-Craig says the study has taken on a new urgency in recent years. "We think the effects of the gene have become more concentrated with each passing generation," he says. "Back in Pastor Kavel's day it might have affected one in 500 who had the gene, but now it's more likely to be one in 80."

A look at just one of the families affected by the gene indicates how widespread the problem may have become. Tony Semler, a retired electronics technician living at Nairne in the Adelaide Hills, is a 6th generation descendant of Georg Eckert, who migrated to South Australia from Prussia soon after Pastor Kavel.

"We're descended from about half of Europe, but most of our family line comes from Silesia," says Tony, who has become an ardent student of genealogy since he was diagnosed as having inherited the FH Morocco gene. "Genealogy can become like an infectious disease," he jokes. But the impact of FH Morocco is no joking matter for his family. Tony had his first heart attack at the age of 34 and has had coronary bypass surgery. His father died of a heart attack at the age of 53, his paternal aunt died of a heart attack at 65 and all of his six brothers have high cholesterol. The good news is that his mother does not have the FH Morocco gene, and is still hale and hearty, though frail, at the age of 93.

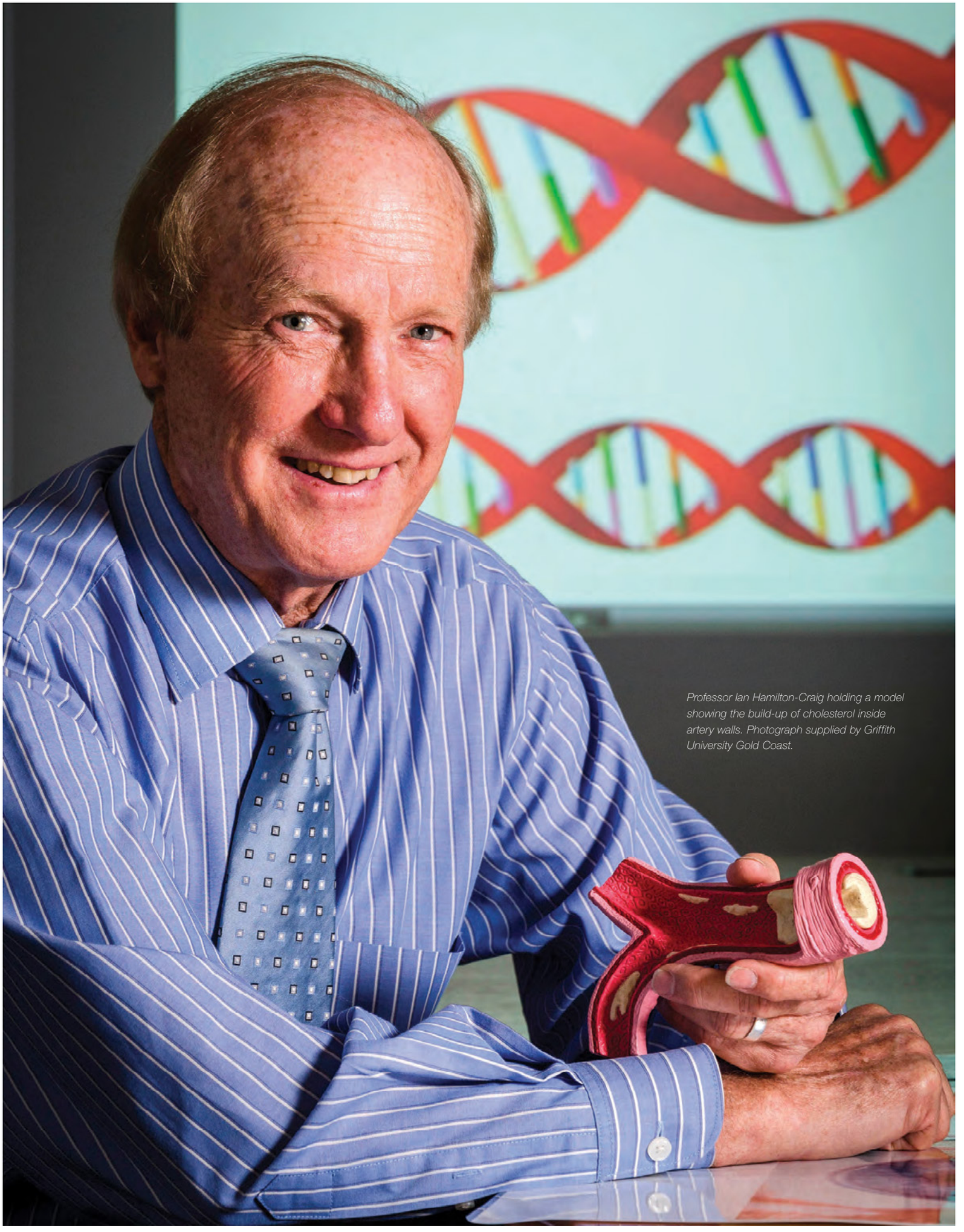
Now a fit and well 67 thanks to extensive medication, sensible diet and exercise, Tony had his DNA sent for analysis and the FH Morocco mutation in his gene coding was detected. Two of his four children have been checked and neither has the errant gene, though one does have high cholesterol. Tests are yet to conclude on his other two children.

Prof Hamilton-Craig estimates that George Eckert and his brother Martin alone now have around 4,000 descendants living in Australia – many of them are still in the Barossa.

Tony Semler says they did a family count in 1960 and found they had 201 first cousins. A book on the Semler family lists close to 2,000 members with Silesian heritage.

"From what I can gather, this gene came into our family line through the Klingberg family many years ago. And what came in as a single strain now seems to be sending tentacles in all directions," he says.

What Prof Hamilton-Craig hopes to determine is whether there is what's known



Professor Ian Hamilton-Craig holding a model showing the build-up of cholesterol inside artery walls. Photograph supplied by Griffith University Gold Coast.

"People of Silesian descent have a unique opportunity to not only improve their own families' future cardiac health, but also to contributue to the health of the wider community," says Prof Hamilton-Craig.

The Semler family in the 1950s.

as a 'founder effect' at work in the Barossa. This occurs when immigrants carry a gene mutation into an isolated community and marry within that community.

"We think the Barossa provides a classical background to this founder effect because this particular Lutheran community remained relatively isolated in the 1800s and early 1900s," he says.

"There was a rapid population explosion after settlement, intermarriage between Lutherans was encouraged, there was little migration to outside areas and a strong tradition of religious beliefs, language and lifestyle was maintained into the 1900s."

So what does all of this mean for people of German descent in the Barossa?

"We know the FH gene exists – in fact it's the most common single gene disorder in our community, affecting about one in 300 people," says Prof Hamilton-Craig.

"In fact it's more prevalent than type 1 (insulin-dependent) diabetes. We know it's a potentially lethal gene that causes premature heart attack, and it's likely to be more prevalent in the German community – especially for the thousands of descendants of the Ekert brothers.

"Even more important, it's easily detected and readily treated, enabling most people to have a normal life expectation. For some people it will enable them to be the first person in their family to watch their grandchildren grow up."

According to the Barossa Family Heart Study website, identifying people carrying FH is vitally important and the team is keen to hear from anyone who suspects they might be a carrier – adults and children over five can be screened.

"At least 80 percent of FH cases in Australia are currently undiagnosed and less than 10 percent are being adequately treated," say the authors. "Early detection and treatment of individuals with FH can delay or prevent the onset of remature coronary heart disease."

Preliminary studies suggest that because of the inheritance pattern of FH, the identification of a single, confirmed case of FH indicates potential new cases in the extended family. For each affected individual, at least one of their parents will be affected, as will approximately 50 percent of their children and approximately 50 percent of their siblings.

Gawler GP Dr Mark Reid, who has known Prof Hamilton-Craig professionally for around 30 years, was one of the first to support the study by making his clinic's cholesterol testing results available.

He says that while it's important that everyone considers their general lipid (cholesterol) level, it was especially important if they are a distant descendant of the Ekert brothers.

"It's unlikely to have come onto the radar of individual GPs because the numbers were too small," Prof Hamilton-Craig says. "We are enormously grateful for the cooperation from the GPs in the area, and we're looking at collaborating with Rotary, which has offered support through its screening programs."

Those identified with high cholesterol will be asked a series of questions which may indicate inheritance of the FH gene and, if so, then a DNA analysis will determine its presence or otherwise. If FH Morocco is detected, immediate family members will also be contacted to undergo the same procedure – a process called cascade family screening.

Over the next two years it is intended to carry out a pilot FH cascade family screening program specifically designed for general practice, being the most cost-effective means of identifying affected relatives.

Early identification of FH allows early and effective treatment to lower cholesterol levels, thereby improving life expectancy and reducing the burden of cardiovascular disease.

"People of Silesian descent have a unique opportunity to not only improve their own families' future cardiac health, but also contribute to the health of the wider community," says Prof Hamilton-Craig.

Tony Semler, one of the first to contribute to the study, says he would definitely urge anyone – especially those with a Silesian genetic background – to get checked.

"It's not a case of being concerned or alarmed," he says, "just a matter of being aware."

To register for the Barossa Family Heart Study download a questionnaire from www.barossaheart.com. If you are concerned about your cholesterol level visit your GP.