

hen he is not searching for a vaccine to combat the Aids virus, Profesasor Sir Andrew McMichael enjoys skiing, walking

and climbing mountains.

His route to the top in science has been an exciting but long climb – requiring much patience and determination which led him to become part of the world-famous Oxford Clinical School.

Professor McMichael said: "In 1983, Sir David Weatherall approached the Medical Research Council (MRC) with the suggestion that a small institute could be developed in the Oxford Clinical School to apply the techniques of molecular and cell biology to study human

"From those small beginnings with a few researchers, which fortunately included me, it has become extraordinarily successful. It now employs over 450 clinical and non-clinical scientific, technical and support staff from all over the world. The visiting scientists and students come from more than 24 countries.

'Recent advances in molecular and cell biology have enormous potential for medical research and practice," Professor McMichael added.

"Initially they were most successfully exploited for determining the causes of genetic diseases and how to control them. Now gene technology is revolutionising all aspects of medical research, advancing understanding of disease, diagnostics, treatments and approaches to vaccines.

'It has spawned a biotechnology industry and should help us gain insights into broader aspects of human biology, including development, ageing and evolution.

Professor McMichael was born in London in 1943. He grew up in Richmond and went to St Paul's School. Medicine was in his blood.

"My father Sir John McMichael was a renowned cardiologist and met my mother, Sybil, when he was working at Hammersmith hospital. She was working as a radiographer at the time," Professor McMichael said.

"My grandfather was director of the Royal Postgraduate Medical School. He pioneered research into the causes of heart failure and developed diagnostic methods which underlie many modern treatments of heart disease.

"From an early age medical research was part of everyday conversation and my brothers and I met his medical friends when they came to dinner. We visited the hospital a lot, including Christmas morning when my father would go to the cardiac ward to carve the turkey," Professor McMichael recalled.

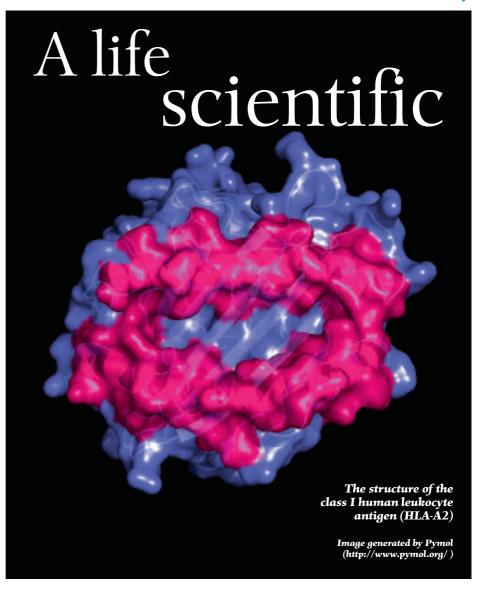
"It was not a given that I would follow in my father's footsteps but he was a huge influence on me. I thought he lived an exciting life. But, when I decided to go into medicine, I determined not to follow him into cardiology too large an act to follow.'

In 1962, Professor McMichael headed for Cambridge and Gonville and Caius College to read medicine.

"At that time the gender balance was about nine-to-one males to females. It made for a pressure-cooker environment concentrating on work. I made good friends there, but girlfriends had to come from London.'

While at home in London on holiday a school friend, introduced him to wife-to-be Kate.

"Our relationship developed quickly as we



Sylvia Vetta meets Professor Sir Andrew McMichael, Oxford University Professor of Molecular Medicine

shared a passion for walking and climbing,"

Kate added: "Our first date was at Harrison's Rocks, a rocky outcrop near Tunbridge Wells. I knew that if I did not get up the climb I did not stand a chance with Michael. I did it!"

After Cambridge, Professor McMichael went to St Mary's at Paddington for three years clinical training. He married Kate in 1968.

As a young house doctor Professor McMichael gained experience in different fields of medicine, including a short locum house job in neurology with Sir Roger Bannister at St Mary's.

'During these three years I worked one night on and one night off and one weekend in two,"

Kate said: "He was known for falling asleep at dinner parties after a night 'on'

Kate had a demanding job teaching in Tower Hamlets. She said: "If you watched Call the Midwife you'll have an accurate picture of the area as it was then. It was hard work, with 40 children in my class.

Professor McMichael said: "We managed to buy a flat in Primrose Hill. My first month's salary cheque of was £80, so it seemed an

outrageous price at £6,000." said Professor McMichael.

When I passed my membership exams for the Royal College of Physicians, it felt like a gateway to a life-long career had opened. But it was a chance event which led me into immunology.

Kate was pregnant with Fiona and was attending the ante-natal clinic at St Mary's. When I went to pick her up, I bumped into the distinguished scientist and Professor of Medicine there, Sir Stanley Peart. He asked if I was looking for a job and wondered if I was interested in research.

'I said I was but did not want to follow my father into cardiology. I was interested in the immune system, one of the few areas my father knew little about! He offered to introduce me to a colleague at the National Institute for Medical Research in Mill Hill and recommended that I put my clinical training on hold and concentrate on research full-time."

That colleague was Ita Askonas, a distinguished Canadian scientist, and she became Andrew's PhD supervisor along with

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Alan Williamson. "In 1974, I obtained a PhD in Immunology at Mill Hill. Ita and I became very good friends and remained so until she died last year aged 89. She helped me a lot throughout my career.

"At that time, we knew about basic antibodies and simple vaccinations but ninety per cent of what we now know about the immune system we have learned since 1974.

"Then, we were just learning that T cells, which develop in the thymus, a lymphoid gland in the chest, are responsible for graft rejection. Now we know that they control virus infections and most types of immunity."

After Mill Hill, Professor McMichael wanted to connect his research to something clinical and learned that Professor Hugh McDevitt from California was working with Oxford geneticist Walter Bodmer on tissue types, specifically something called HLA.

Professor McMichael said: "If you have the wrong HLA tissue type you will reject organ grafts. Almost everyone not closely related has inherited different HLA types so this has been a big problem in transplantation. HLA types are highly variable and complex.

"In 1973, it had been discovered that some diseases, such as one type of arthritis, were more common in people with particular HLA types. I decided that was the area I wanted to research," Professor McMichael said.

"The obvious thing to do was head for California to work with Hugh. There, we had the time of our lives. I worked in a stellar scientific environment and also enjoyed spending weekends with Kate and our two older children outside in the perfect climate, camping in places like Yosemite Valley.

"In 1976 I was offered a permanent job at

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Stanford University and it was very tempting. But we had a lot of family in the UK and we felt this is where our roots were and we would be more connected with the rest of the world in the UK compared to California — at least in those pre-Internet days."

Professor McMichael was taking a big risk in deciding to come back to the UK. The post in California was permanent, well-paid and with good prospects. He returned to the UK in 1977 with a guaranteed of just 12 months employment with a grant from the Wellcome Trust to work in Oxford.

"My first grant was used to look at the role of T cell immunity in influenza virus infection working once again with Ita Askonas," Professor McMichael said.

"I am lucky that things worked out so well. In 1977, the Nuffield Department of Clinical Medicine had four or five senior scientists and now it must have 300.

"The expansion has been huge. The Oxford Medical School began in a wing of the Old Radcliffe Infirmary and moved to the John Radcliffe in 1979 and, in 1989, the Weatherall Institute was built on the JR site.

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"When John Bell became Regius Professor, he wanted to build a new Institute of Medical Genetics on one of the car parks. As that was not possible he turned his eye towards the green fields at the Churchill. The result is there for all to see."

Professor McMichael now works in one of the new institutes on that site.

"I found myself working with extraordinary people like David Weatherall, Peter Morris (Professor of Surgery) and later John Bell (Regius Professor), so the gamble of returning paid off," Professor McMichael said. "I have been fortunate to be part of the extraordinary growth of clinical research in Oxford.'

Andrew showed me a beautiful picture which he explained was of an HLA molecule.

"Some American scientists Pamela Bjorkman, Jack Strominger and Don Wiley were able to make this image of the crystal structure of an HLA molecule. This is the top end view and is magnified over a million times."

He pointed to a small area of pink.

"These are the peptide fragments of cellular proteins, which would include virus peptides if the cell was infected. From my perspective, this is the most influential paper in immunology of the last 50 years.'

"Following this paper the study of human immunology took off across the globe. I was by then focusing on HIV, looking at why some people do better than others.

"Ône thing shown by the HLA crystal is that all the genetic variability in HLA occurs around the groove that binds the peptides. Therefore, different people respond to a virus, such as HIV, in different ways and indeed people with certain HLA types have better resistance to HIV.

This information is central to our design of the HIV vaccine we are developing in Oxford," Professor McMichael said.

Much of Professor McMichael's vaccine development programme is funded by the Centre for HIV Vaccine Immunology - the CHAVI programme – which is based at Duke University in North Carolina and funded by a grant from the US National Institutes for Health.

This is a very intensive collaborative programme," he said. "I have international telephone conferences two-or-three times a week and visit the US six-times-a-year, working with a very exciting group of scientists with different areas of expertise.

'Science is a global activity, all conducted in the English language, and Oxford is very well connected internationally. Besides our overseas collaborations, we have scientists who come here from all over the world. I love that aspect of my work.

In addition to his HIV work, Professor McMichael also keeps up an interest in influenza. Given the constant threat of a new influenza virus pandemic, he is also working with the MRC and the Wellcome Trust on the flu-watch programme, monitoring influenza virus infection in 2,000 healthy volunteers.

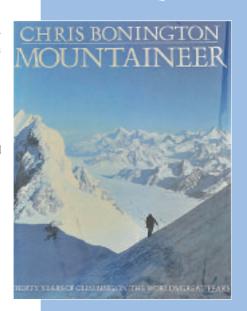
The study is designed to determine whether pre-existing T cell immunity protects against natural influenza virus infection.

Structure of the human class I histocompanibility SIR Andrew McMichael became a professor in 1981 and set up the Medical Research Council Human Immunology Unit in 1998, retiring from the post of director three years ago. In 2005, he became director of the Weatherall Institute and when he retired from that post, in 2010, it employed 400 people.

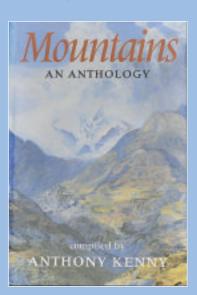
> His work has been recognised by Fellowship of the Royal Society in 1992, Fellowship of the Academy of Medical Sciences in 1998 and a knighthood in 2007.

He also holds honorary Fellowships at Trinity, Corpus Christi and Harris Manchester Colleges and Honorary Degrees from the University of Zurich and Imperial College, London.

The paper in Nature which is Professor McMichael's desert island choice. "Science is often thought to be esoteric and inaccessible, but this paper and the image therein shows that science too can be beautiful," he said



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Above and left, Professor McMichael's favourite mountaineering books

"Because of the threat of Avian flu we have also developed very strong links with Beijing and there are senior Chinese scientists working here with us on the immunology and cell biology of influenza," Professor McMichael said. "These collaborations with China are particularly exciting."

Away from the lab, Professor McMichael

maintains his love for the great outdoors.

He said: "We bought a house in France seven years ago and go there about five times a year. We ski in the winter and walk in the summer.

Professor McMichael showed me a picture of his old farm house in La Salle les Alpes and some of his mountaineering books including an old edition of Scrambles in the Alps by Edward Whymper, the first man to climb the Matterhorn.

Professor McMichael said: "Once on the top, Whymper looked at the wonderful view from the summit towards the south west and the mountains near our French house (the Pelvoux, Ecrins and Meije) which he described as his first love. He opened up the sport of mountaineering in that area and they have even built a statue of him near the village it is unusual to find a statue of an Englishman in France.

"B ut my favourite mountaineering book is probably this one ..." Professor McMichael showed me Mountains: An Anthology by Antony Kenny who was pro-vice chancellor of the University of Oxford from 1984 to 2001.

We had reached the time when Professor McMichael would have to select his deseert island item. After much thought he decided on the Nature paper by Pam Bjorkman and colleagues, containing the ground-breaking crystal images.

He said: "Science is often thought to be esoteric and inaccessible, but this paper and the image therein shows that science too can be beautiful. This crystal profoundly influenced all my scientific thinking over the last 27 years."