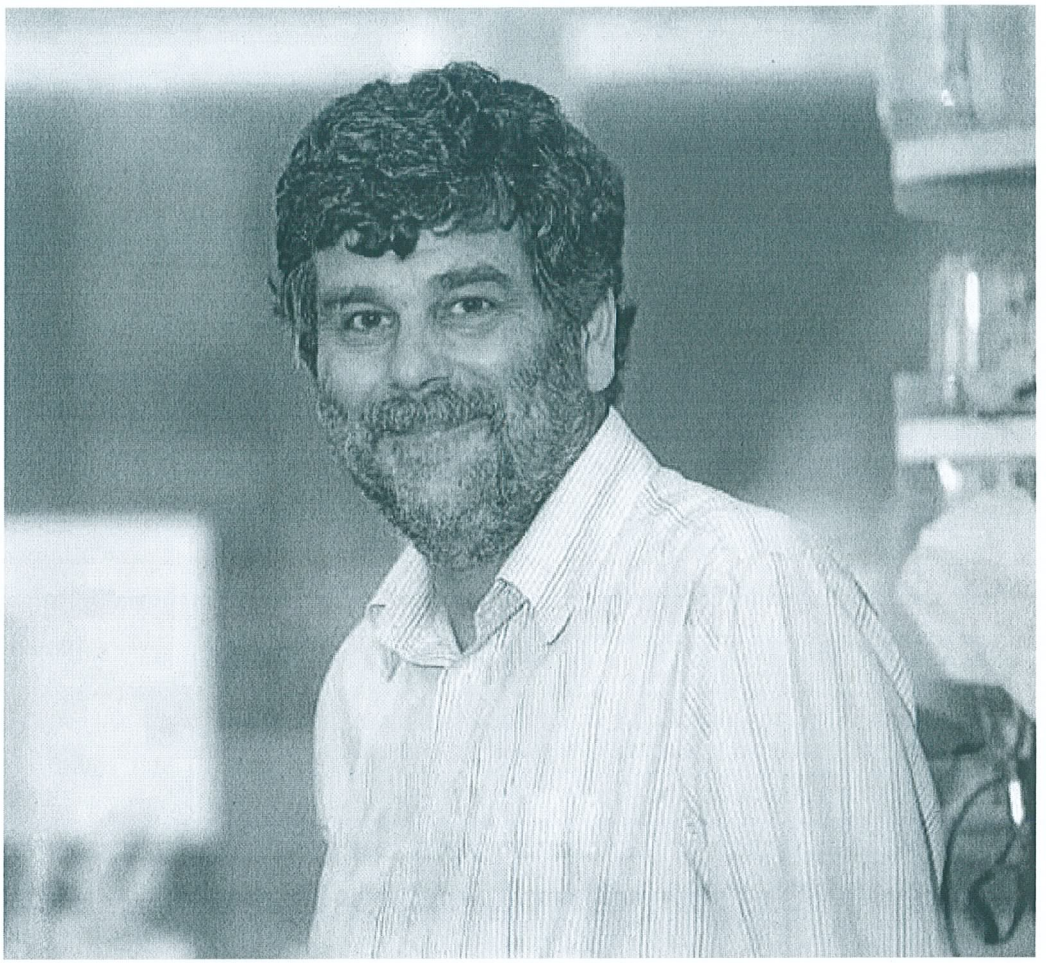
Of mosquitoes, parasites and man

Professor Christian Doerig enjoys a challenge, having left the world of viruses behind in the '90s for the neglected field of malaria research. Recently, he left his tenured position at INSERM in Switzerland for Melbourne to take up the role of Head of Department of Microbiology at the School of Biomedical Sciences, and also set up a new lab.

Professor Doerig talks to *Biomed Benchmark* about malaria and his new appointment.



Professor Christian Doerig.

Malaria is an infectious disease involving complex relationships between three parties. A parasite called *Plasmodium falciparum* hitches a ride on the *Anopheles* mosquito, which draws blood from an infected person. Inside the mosquito, malarial parasites develop and accumulate in the insect's salivary glands, and are then transmitted to a new human host during the next meal. There, the parasite invades and replicates in the liver, then infects red blood cells, where it proliferates with deadly results, killing one million people each year predominantly in developing countries.

Professor Doerig studies the molecular switches that trigger the deadly asexual replication of malarial parasites in human blood. He is interested in a family of enzymes known as protein kinases, which regulate cellular growth and proliferation by modifying other proteins in a process called phosphorylation.

After the *P. falciparum* genome sequence became available, Professor Doerig used bioinformatics approaches to show that 85 genes encode the parasite's protein kinases. Recently, he led an international team that revealed which of these genes are essential for the parasite's survival in red blood cells.

"We now know that 36 kinases are crucial for the parasite to proliferate in humans," Professor Doerig says.

"Also, with Professor Andrew Tobin, from Leicester University in the UK, we identified several hundred phosphorylation sites on *Plasmodium* proteins, and demonstrated for the first time that tyrosine phosphorylation occurs in the parasite on regulatory sites of kinases, work that was published last month in the prestigious journal *Nature Communications*."

From a treatment perspective, it may be possible to develop selective inhibitors of these important malarial enzymes.

"We can now screen molecules to find inhibitors of these protein kinases," says Professor Doerig, who will collaborate with Professor Andrew Wilks (Monash Institute of Medical Research), Dr Isabelle Lucet (Department of Biochemistry and Molecular Biology), Professor Brian Cooke (a malaria researcher at the Department of Microbiology) and GlaxoSmithKline, a pharmaceutical company that has a 'malaria box' containing 13,500 compounds that kill malaria parasites. He hopes that novel kinase inhibitors will be found among these drug-like compounds with anti-malarial activity.

"As the malaria parasite quickly develops drug resistance, we need a constant pipeline of new antimalarials with different modes of action," Professor Doerig says.

"Kinase inhibitors represent one approach. However, it's likely that the parasite will also become resistant to them. So even if we are successful, the story won't end here."

Aside from his malaria research, Professor Doerig is leading the Department of Microbiology, where scientists study pathogenic bacteria, viruses and parasites. While it's early days in the job, his goals are clear.

"I want our basic research to have a clinical impact in the long term," he says.

"Drug and vaccine discovery are dependent on understanding how pathogens proliferate and interact with human or animal hosts. Therefore, I wish to build on the strong fundamental research skills from our Department and support translational projects with university, industry and clinical partners.

"There are also opportunities for synergistic interactions with other School departments in the areas of structural biology and developmental biology."

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