PHARMACOGENETICS OFFERS HOPE

A recently returned award-winning medical scientist is stirring major excitement in South Africa with a pharmacogenetic approach to drug therapy in general, and to AIDS in particular. The latter has the potential to radically reduce drug-resistant strains of the HIV virus through viral genome sequencing.

Some development of drug-resistant strains in the HIV-positive population is considered inevitable in spite of the best managed antiretroviral roll-out systems because of South Africa’s demographics, infrastructure, and lack of human resource capacity.

Vital significance

The cost to the State of bulk supplies of second-generation antiretroviral drugs would be huge and has been the subject of fierce debate around the current preparedness for and pace of the drugs roll-out. This confers vital significance on the work of University of Cape Town medical graduate, Professor Michael Pepper, who recently joined the Witwatersrand School of Anatomical Sciences from the University of Geneva.

Pepper stirred major interest at a Roche Diagnostics In Vitro forum in Johannesburg in October by, among other things, suggesting that in the not too distant future a failure to genotype patients before any treatment could be considered unethical.

In his presentation, Pepper said that useful South African statistics for adverse drug reactions (ADR) were absent. However, in the USA 100 000 people died annually from ADR and more than two million hospital patients experienced ADR every year.

United Kingdom statistics showed ADR to be costing R3.8 billion per annum, with 7% of all patients affected.

ADR accounted for an estimated 10% of National Health Service (UK) bed days while chemotherapy ADRs increased overall drug costs by 15%.

Financial backing

At the time of writing, Roche Diagnostics were in the process of setting up a multi-million rand cutting-edge molecular diagnostics research platform for Pepper.

He is due to brush up on some technology in the USA before beginning his research in earnest this year.

It will be South Africa’s first public-private partnership in this area. While genotyping and resistance testing is some way off, Pepper’s current work centres on drug toxicity and therapeutic levels – how the patient metabolises the drug and the implications this has for medicine. He told the Johannesburg diagnostics forum that educating health care professionals about rapidly evolving molecular technology including the human genome was essential so that it could be incorporated into clinical practice as soon as practically possible.

Pepper told Izindaba that a great deal of work had been done on viral resistance, especially around relating mutations of the HIV genome directly to different kinds of drugs. However, ‘very little’ work around therapy had been done on the patient genome. Asked when he thought his work might begin to have direct benefit, Pepper said, with typical scientific caution, ‘that’s impossible to answer right now.’

He explained that sequencing the viral genome enabled scientists to tell whether a particular virus would become resistant. Mutations in the drug targets in the virus were predictors of whether there would be resistance or not. ‘Practically, you take a blood sample and when you do the viral load you take some DNA from the virus and perform the sequencing in any one of a number of ways’.

Pepper said there had been ‘enormous excitement at universities and in the public and private pathology sectors’. He said that two genes, the reverse transcriptase gene and the protease gene, underwent a large number of mutations, often in response to sub-optimal treatment, which conferred resistance to some of the AIDS drugs.

‘These are the things we’d want to sequence and, depending on the mutations in these genes, we’d be able to predict to which drugs the virus would be resistant,’ he said. This was done through algorithms that were constantly updated in public databases.

He added that the ‘other side of the coin’ was to examine the patient to see whether or not they would respond to antiretroviral and other drugs used in the treatment of the complications of AIDS. Many of these drugs, including antiretrovirals, caused severe and sometimes life-threatening side-effects.

Slow and fast metabolisers

People metabolise drugs at different rates. For slow metabolisers there could be a therapeutic effect but a greater risk of toxicity, whereas rapid metabolisers
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The core business of the HMPG is to produce 17 periodic medical publications in about 100 editions annually with content generation by a highly skilled and experienced editorial team. This team will remain directly accountable to the South African Medical Association (SAMA).

However, with some lateral thinking, a deal has emerged in which the HMPG business team (production, marketing, advertising, distribution) will partner Andrew Fehrsen, founder and MD of one of the country’s largest business to business publishing houses, Cape Media.

Replacing institutional memory and specialist hands-on ability like that which Roberts has was never going to be an easy task, yet the current deal will open even more doors and optimise the HMPG operation.

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