Pharmacogenetic screening of Indigenous Australians

To the Editor: A daunting idea for health care providers is the statistic that, for many medications, only about half of the patients given

standard doses will receive the desired therapeutic benefit.[1] In the past decade or so, it has been argued that some of this variation in response may be attributed to genetic differences between individuals in mechanisms responsible for the pharmacokinetics and pharmacodynamics of many drugs.[2]

The disparity in health standards among Aboriginal and Torres Strait Islander people compared with non-Indigenous groups is a cause for concern, and requires a concerted political effort to instigate adequate solutions.[3,4] Some of the problems include a higher rate of diseases such as hypertension, diabetes, obesity, cardiac disease and depression.[3,4]

The range of medicines prescribed for these conditions is broad, and some people may not receive the full therapeutic benefit, or may have more severe side effects compared with others. Genetically determined variables contribute to the pharmacokinetics and pharmacodynamics of these drugs. Many medications used to treat such diseases are metabolised by the cytochrome P450 (CYP) hepatic enzyme systems, and/or their pharmacokinetics are altered by drug influx and efflux systems. Many of these mechanisms are under genetic control and their efficiency may vary between individuals.

Despite this, there are few data on the pharmacogenetics of Indigenous populations generally, and the data on Aboriginal and Torres Strait Islander populations are particularly scant.[5] Of the few genetic studies of Indigenous Australians, one found that CYP2C19 and CYP2D6 allele frequencies in a group from remote north-western Australia differed significantly from those for Australians of European ancestry, but were similar to those for East Asian populations.[5] An altered CYP2C19 allele could mean alterations in levels of drugs such as phenytoin and clopidogrel, and an altered CYP2D6 allele could mean alterations in levels of drugs such as tricyclic antidepressants, selective serotonin reuptake inhibitors, codeine and tamoxifen.

We urgently need to identify clinically relevant issues relating to the capacity of people from these groups to metabolise certain medicines. Screening for genetic variations in drug metabolism and transport mechanisms may highlight significant variations in capacity. This may influence whether people benefit from or are harmed by commonly prescribed medications for hypertension, type 2 diabetes, cardiac disease and depression.

The high and increasing prevalence of these diseases among Aboriginal and Torres Strait Islander populations supports a detailed, methodical assessment of the genetics of their drug-metabolising capacity.

Joseph D Tucci Senior Lecturer

Pharmacy Department, La Trobe University, Bendigo, VIC.
j.tucci@latrobe.edu.au

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> “genetic variations in drug metabolism ... may influence whether people benefit from or are harmed by commonly prescribed medications” Tucci