Pharmacogenomics deals with genetic variations that influence the response to medicines via metabolism, transporter and receptor polymorphisms and in a few cases has led to clinical translation. Analgesics, especially opioids, antiemetic and antidepressant drugs show marked interpatient response variability in both efficacy and adverse effects and this can be due to pharmacogenomic factors.

The cytochrome P450 2D6 poor metaboliser phenotype reduces the effects of some opioids such as tramadol, whereas in ultrarapid metabolisers adverse effects are seen with codeine and the antidepressants, but enhanced efficacy to tropisetron.

The efflux transporter p-glycoprotein located at the blood brain barrier limits access of these drug classes to the brain; genetic polymorphisms result in enhanced efficacy but also adverse effects to many of these drugs. For opioids, the major mu receptor polymorphism leads to reduced effects in some settings but has not been proven in large patient studies.

The role of opioid-immune signalling polymorphisms remains to be studied; however, the complexity of individual pain responses to treatment likely limits a major role for individual candidate genes whereas epistasis and epigenetics studies may be more beneficial, and need to be investigated.

Thus a source of interpatient variability in response to these major palliative care classes of drugs can in some cases be attributed to the patient’s genetic profile that controls drug metabolism, transport out of the brain, target site and receptor signalling. These might help to explain at the bedside why some of the drugs “don’t work as well” or “work too well”.

Pharmacogenomics: Implications for palliative care practice. Andrew Somogyi, Discipline of Pharmacology, University of Adelaide

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