Differential activity of efflux transporters of the model eukaryote *Dictyostelium*

The amoeba *Dictyostelium discoideum* inhabits soils, tracking bacterial and yeast prey through chemotaxis, and has a complex life cycle encompassing unicellular and multicellular stages. It has become a useful eukaryotic, biomedical, and cell biology model organism for phenomena from cell-type differentiation to signalling to phagocytosis. These social amoebae retain many similar genes to those of the human genome, including for the evolutionarily ubiquitous multidrug and efflux (MATE) transporters. Despite large multigene MATE families in some organisms, man and *Dictoystelium* both encode a pair. Each human MATE operates in specific tissues including the kidney and liver, and can facilitate cancer drug resistance. Their transcription in the model amoeba suggested one is more highly expressed and differentially regulated, with upregulation following 'test drug' treatment with polyphenolic secondary metabolites. The second MATE was upregulated most, and appeared to be the principal transporter of the pair, when toxin efflux was required. Fluorescence reporter visualisation confirmed the predicted plasma-membrane location in the unicellular amoeba. Genetic and biochemical ablation of each did not affect viability but diminished phagocytosis of prey bacteria and reduced the internal concentration of the polyphenolic treatments. Imaging and LCMS also confirmed MATE activity was efflux, not import. The function of these transporters has not been considered previously in multicellular *D. discoideum,* the sentinel cells of which were reported to sequester and remove toxins to the extracellular matrix which is left behind the moving 'slug'. It is also of interest when testing drug activity in this model organism.