New research looks at novel ways to combat drug resistance

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University of Southampton biological scientists are leading a major research project aimed at making drugs more effective.

They are investigating a group of proteins called 'multidrug transporters', which remove unwanted and toxic material from cells. Normally these proteins protect cells from toxins, but multidrug transporters also prevent anticancer drugs from killing cancer cells, particularly since the amount of these proteins is increased in cancer cells when they encounter such drugs. Related proteins also remove antibiotics from bacteria and remove herbicides from the plant cells of weeds leading to herbicide resistant weeds.

All cells are surrounded by a membrane made of molecules called lipids, which forms a barrier that prevents the movement of many important biological molecules into and out of the cell. Embedded in this barrier are proteins that provide the cell with the ability to take in nutrients and remove waste and toxic molecules.

Dr Malcolm East, a Reader in Biochemistry, who is leading the research with Dr Howard Barton, a Reader in Biochemistry and Molecular Biology, says: "Besides ejecting waste material, cells also remove drugs, which make them less effective as treatments. We believe that a particular group of lipids, called anionic lipids, within cell membranes play a role in controlling the biological function of certain membrane proteins. We want to know how lipids interact with proteins and how that affects their ability to transport drugs.

"Understanding these mechanisms could suggest ways of improving the effectiveness of antibiotics, anti-malarial drugs and cancer treatments and boost the action of herbicides and pesticides."

Anionic lipids in the membrane change in amount and distribution when cells respond to changes in their environment. By labelling different proteins and lipids, the scientists can determine which lipids have a closer relationship with the multidrug transporter and how it affects the drug transporting ability of the protein.

Dr Barton adds: "These studies will tell us how signals are transmitted to membrane proteins by changes in membrane lipid composition and distribution.. In addition a greater understanding of how multidrug transporters are controlled by lipids, may suggest ways in which these proteins can be controlled by the use of novel drugs that would also interact with these multidrug transporters. This could help to tackle treatment failures caused by the serious problems of antibiotic resistance in bacteria and resistance to anticancer drugs seen with repeated rounds of chemotherapy. A similar approach could be taken to provide strategies for reducing the resistance seen with a whole range of important molecules, including pesticides, herbicides and anti-malarials."

Dr East and Dr Barton have won £287,000 from the Biotechnology and Biological Sciences Research Council (BBSRC) for the three-year project.

Provided by University of Southampton