'First step' to perfect drug combinations

October 23 2011

The researchers found a way of identifying ideal drug combinations from billions of others which would prevent inflammation from occurring.

The findings, published in *Nature Chemical Biology*, could be the first step in the development of new drug combinations to combat severe diseases and conditions.

Most non-infectious disease, such as cancer, stroke and Alzheimer's are worsened by inflammation, which is the body's natural defence mechanism.

Inflammation has evolved to help fight infection but can also be very damaging in long term disease, prolonging suffering and ultimately risking premature death.

After a stroke, the body reacts to the injury as if it were an infection, causing further damage. By blocking the inflammation, the chances of survival or higher quality of life following a stroke are thus greatly enhanced. This can be achieved by quickly and effectively identifying combinations of drugs which can be used together.

Existing 'clot-busting' stroke drugs are only effective if administered within three hours after the stroke – often very difficult to achieve as people are often unaware they are having a stroke – and even then do not completely solve the problem, often leaving sufferers with serious disabilities.

However, using ideal drug combinations the researchers suggest they can block inflammation and therefore greatly reduce the damage caused by non-communicable diseases such as stroke.

Although the researchers have initially concentrated on stroke, they believe the process can be applied to all drugs and for a huge variety of diseases.

The multi-disciplinary team of researchers, led by Professor Douglas Kell, Professor of Bioanalytical Science at The University of Manchester, developed an evolutionary computer programme which rapidly sifted through nine billion different combinations of potential drugs.

Sorting and testing 50 drug combinations at a time using robotics in the laboratory, the scientists were able to find effective combinations and then refine them as many times as necessary to find ideal combinations.

Ultimately, they hope this will lead to the development of tailored therapies for treating inflammation.

Professor Kell, who is also Chief Executive of the Biotechnology and Biological Sciences Research Council, said: "Most diseases have complex causes. This makes their analysis a problem of systems biology, and to find novel therapies multiple targets need to be attacked at once.

"We have devised a strategy, based on Darwinian evolution, to make this considerably easier. Although our immediate interest is inflammation and conditions such as stroke, our approach is universal and is thus applicable to all complex diseases."

Another advantage of choosing ideal drug combinations is that it allows patients to take smaller doses, which reduces potential toxicology

concerns.

Professor Kell and his team worked with computer scientists at the University to create the programme. Professor Pedro Mendes explains: "Our experiments were guided by software that is based on an evolutionary algorithm. The algorithm suggests new drug combinations from previous ones by re-mixing their components – much like the DNA of a child is a mix of that of their parents.

"The new drug combinations are then tested and the best are selected to continue generating new ones. In each experiment we tested 50 drug combinations, then the software would tell us which new ones to test in the next experiment."

Provided by University of Manchester