Tumour survival tactics tackled by researchers

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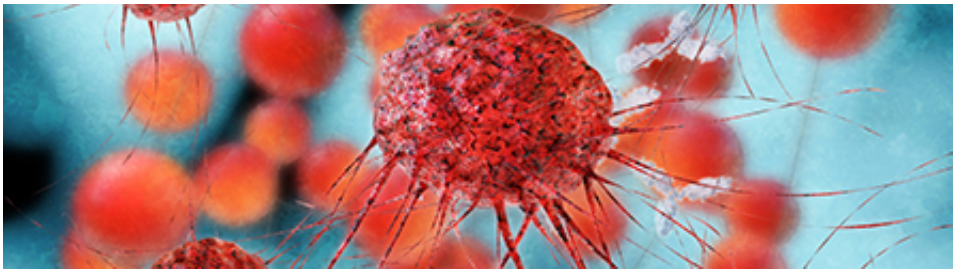

Credit: University of Nottingham

Scientists at The University of Nottingham are tackling a tumour survival mechanism that has left experts baffled for more than 50 years.

Their research – the culmination of 10 years of work – has revealed how cancer cells develop a resistance to the drugs prescribed to kill them in a tactic similar to antibiotic resistance.

The results of their study, published in the journal *Seminars in Cancer Biology*, could lead to new cancer treatments and drugs against which tumours will be unable to develop immunity.

Every year, around eight million people die from cancer worldwide. While huge strides have been made in the development of new chemotherapy treatments, the effectiveness of these treatments could be compromised by the development of multi drug resistance (MDR) in

cancer.

MDR is a unique phenomenon that happens when, after an average of five years of anticancer treatment, cancer cells are able to fight off anti-cancer drugs.

One of the most puzzling aspects is that once MDR cancer cells are resistant to a single type of anticancer drug, they become resistant to nearly all other treatment drugs too in a similar process to how bacteria build resistance to antibiotics.

It is believed that once cancer cells are exposed to one type of drug for too long, they become 'immune' to that particular drug. Inside the tumour are different groups of cells that are not all identical and some of these cells may have a mutation that makes them resistant to the anticancer drug.

Over time, the drug will appear to be working as the non-resistant cells are destroyed and the tumour shrinks in size. However, as only resistant cells are left within the tumour, the drug becomes ineffective and relapse becomes inevitable.

This resistance is considered an evolutionary process in which tumour cells acquire mutations to allow them to survive.

While this single drug selection process can explain how cells are resistant to a drug – or even similar anticancer drugs that belong to the same family of drugs – it cannot explain how one mutation can impact of hundreds of chemically unrelated drugs.

The latest study, involving Dr Cyril Rauch in the University's School of Veterinary Medicine and Science, has gone beyond the usual biological approach to this conundrum – bringing physics into the mix in an

attempt to unpick the phenomenon.

They have found that physics and biology both play an important role in drug resistance and that the concept of 'space' (or 'dimension') is paramount in understanding how this physical specificity to one drug can lead to resistance against multiple drugs.

Dr Rauch said: "So far most studies in the field have concentrated in understanding the relationship between the chemical structure of anticancer drugs and their rejection from cancer cells, by assuming that the 'immunity' would be driven by the drug chemistry. However our team has suggested that the drug chemistry, while important, is secondary to the ability of cancer cells to become impermeable to drugs by changing the physical properties of their membrane (making the membrane stiffer) rendering the anticancer drugs unable to interact with anticancer cells."

In doing, so they have suggested new targets to combat cancer related to the membrane of MDR cancer cells.

More information: Ziad Omran et al. Physical and biological characteristics of multi drug resistance (MDR): An integral approach considering pH and drug resistance in cancer, *Seminars in Cancer Biology* (2017). DOI: 10.1016/j.semcancer.2017.01.002

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