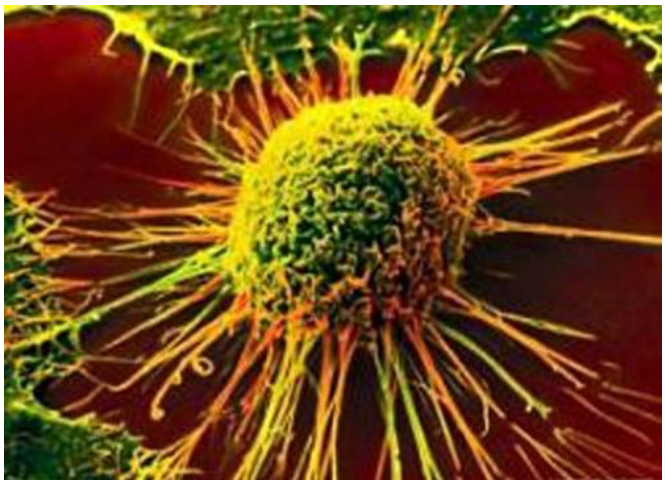
How resistance to a new cancer treatment might be overcome

29 July 2015, by Jamie Brown



A promising agent for the treatment of cancer has so far had little effect on the most common lung tumours, but new research from The University of Manchester has suggested how this resistance might be overcome.

In two papers released in the journal *PNAS*, the research team examined factors which mean that the most common type of lung cancer – itself the most common cause of cancer deaths – is resistant to a cytokine called TRAIL that causes cell death in many other types of tumour.

The researchers found that in non-small cell lung cancer, which accounts for around 85 percent of cases, a small RNA molecule called miR-148a is suppressed in TRAIL resistant cells, but that when used together, miR-148a sensitises tumour cells to TRAIL and results in the tumour shrinking.

Dr Michela Garofalo, from the CRUK Manchester Institute led the research. She said: "Discovering a potential reason why TRAIL is resisted by lung cancer could lead us to new treatments for this particularly deadly form of the disease.

"miR-148a certainly seems to play a role in this resistance, so it's an avenue to explore alongside other factors which influence how the tumours respond to treatment."

In related research also published in PNAS, Dr Garofalo's team discovered another mechanism which makes tumours resistant to TRAIL. NF-?B is a protein which TRAIL itself increases the supply of in resistant lung tumours. By supressing it in cells they found that TRAIL became much more effective at causing tumour cells to die.

"TRAIL is currently in clinical trials for other cancer types," added Dr Garofalo. "But little is known about why non-small cell lung cancer is so resistant. These findings begin to shed light on those unique reasons, and suggest that by inhibiting the factors that cause resistance, TRAIL might become a useful treatment."

More information: "A set of NF-?B–regulated microRNAs induces acquired TRAIL resistance in lung cancer." *PNAS* 2015 112 (26) E3355-E3364; published ahead of print June 15, 2015, DOI: 10.1073/pnas.1504630112

"The tumor suppressor miR-148a improves the response to TRAIL-induced apoptosis in NSCLC," *PNAS*

Provided by University of Manchester