Exploring the Effects of a Novel HSP90 Inhibitor on Colorectal Adenocarcinoma and Oral Squamous Cell Carcinoma in Conjunction with Ionizing Radiation Treatments

One of the toughest diseases to combat stems from the inevitable wear and tear of the human body and its cells. Despite the highly advanced, highly efficient healthcare systems and technologies of the modern world, one disease in particular that is programmed into the very structure of a cell's operation still eludes a complete cure. This ailment is, of course, none other than cancer. As a cell metabolizes, ages, and divides, it accumulates errors and mistakes in its genetic code that, when accumulated in high enough numbers in just the right genes, can cause a cell to bypass a great majority of intracellular or extracellular regulatory signals. These cells, now unrestricted in their ability to multiply and survive, can grow into a dangerous mass with the ability to invade normal tissue and disrupt various processes needed for proper bodily function.

While these anomalous cells may be virtually invisible to the immune system and unresponsive the body's queues to stop their rampant growth, all hope is not lost in halting their progress. The basis of all cellular function relies on the interactions between the numerous proteins expressed within the cell. Since cancers are essentially cells running out of control, they are also more dependent on certain types of proteins than normal cells. One particularly abundant type of protein present in all cells is essential to the proper structuring of other proteins. This protein family is known as heat-shock proteins. Without heat-shock proteins, many of the other proteins that are essential to a cells life would not fold properly and their function would be eliminated, thus causing cell death.

Some forms of cancer seem to be particularly reliant upon these heat-shock proteins for survival which means that they could be used as an excellent target to destroy cancerous cells. Since a type of cancer can rely on these proteins more than a normal cell, a drug can be administered in a specific concentration such that only the cancer cells die and the normal cells survive. Even if this particular effect is not achieved, the drug can still be used in order to weaken the cancer cells enough so that other treatments may be more effective. As with most modern cancer therapies, a cocktail of drugs is used in order to destroy the cell mass along with other external methods such as ionizing radiation. The main focus of this project was to explore a novel, relatively untested, heat-shock protein inhibitor and to determine if it had the possibility of increasing a cancer cell's sensitivity to this widely employed ionizing radiation treatment. Over the course of this project, cells were submitted to various assays to assess changes in survivability, radiosensitivity, cell cycle distribution, protein expression levels, DNA damage repair efficiency, and cell mass structural morphology following treatments with a combination of ionizing radiation and heat-shock protein inhibitor.

Adrian Dascalu

Master's Thesis in Biology: 45 hp, 2012-2013
Biomedical Radiation Sciences, Uppsala University
Supervisor: Bo Stenerlöw, Diana Spiegelberg