

## S28. Innovative Agents in Cancer Prevention

M.M. Manson

*University of Leicester Cancer Biomarkers & Prevention, Leicester, United Kingdom*

There are many facets to cancer prevention – a good diet, a healthy environment, avoidance of carcinogens such as those in tobacco smoke, and screening of populations at risk to allow early detection. But there is also the possibility of using drugs or naturally occurring compounds to prevent initiation or to suppress tumour growth. Only a few such agents have been used to date with any success, and these include non-steroidal anti-inflammatory drugs for colon and tamoxifen for breast tumours. An ideal chemopreventive agent would restore normal growth control to a preneoplastic or cancerous cell population by modifying aberrant signalling pathways and/or inducing apoptosis in cells beyond repair. Characteristics for such an agent would include selectivity for damaged or transformed cells, good bioavailability and more than one mechanism of action to foil redundancy or crosstalk in signalling mechanisms. As more research effort is being targetted towards this area, the distinction between chemotherapeutic and chemopreventive agents is blurring. Chemotherapeutic drugs are now being designed to target over- or under-active signalling molecules within cancer cells, a philosophy which is just as relevant in chemoprevention. Develop-

ment of dietary agents for chemoprevention is particularly attractive because of our long-standing exposure to them and their relative lack of toxicity. The carcinogenic process relies on the cell's ability to proliferate abnormally, evade apoptosis, induce angiogenesis and metastasise to distant sites. In vitro studies with a number of different diet-derived compounds suggest that there are molecules capable of modulating each of these aspects of tumour growth. However, on the negative side many of them have rather poor bioavailability. The challenge is to uncover their multiple mechanisms of action in order to predict their efficacy, to learn how to use them effectively in combination, and in some cases to redesign them to improve potency or bioavailability. These ideas are illustrated by dietary agents such as indole-3-carbinol, epigallocatechin gallate, curcumin and resveratrol, all of which appear to have a number of different molecular targets, impinging on several signalling pathways. Ultimately it may be possible not only to suppress tumours and to extend quality of life by administering isolated dietary constituents, but also to refine the definition of a cancer chemopreventive diet.