Chairperson's Introduction

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Cancer is caused by mutations occurring in genomic DNA that affect several processes such as cell signalling and survival, which cumulatively result in the affected cells growing at a rate faster than they die. This results in the formation of a solid or liquid tumour. In the former case other processes, such as angiogenesis to provide the tumour with nutrients from circulation and to clear it of waste products, invasion of the normal surrounding tissues, intravasation, extravasation and establishment of colonies at distant sites, are all required for spread of the disease.

Molecular biology has uncovered many of the genes responsible for these events and these appear to co-operate to form assemblies which function in normal tissues to allow intercellular signalling which regulates cell division, differentiation and apoptosis to permit tissue pattern formation. Mutation of members of these assemblies can alter the balance of their activities and these changes can be manifest in the occurrence of clinically significant disease. Many of the mutations in genes, while affecting directly the activity of the protein product, also indirectly affect other proteins in the system. An example is the wound healing response where cells respond, for instance, in an epithelium, to local tissue damage by entering or reducing their transit time through the cell cycle, secreting proteolytic enzymes to remove substances such as damaged basement membrane, detaching from their neighbours and becoming motile, all processes required to re-establish the integrity of the epithelial layer. At the same time they secrete factors to initiated neo-angiogenesis at the site of the wound to restore vascular supply. A mutation towards the top of this hierarchy, for example, in a growth factor receptor, can initiate essentially the same complete programme despite the rest of the molecules in the system being normal. Thus it should be of no surprise that activation of the epidermal growth factor receptor in epithelial cells induces them, for instance, to secrete vascular endothelial growth factor. The process becomes pathological however as, while the normal system has signals such as contact inhibition of growth which terminates the programme, in the case of mutations this cannot occur as the process is permanently activated.

The three chapters in the section describe aspects of our knowledge of genes evidently involved at important points in these information cascades, notably cell surface receptors, intracellular signal transducers and apoptotic decision making. All of these are being explored or exploited as targets for anti-cancer drugs and in some cases such drugs have produced useful results. Much more remains to be discovered however but progress is still very evident. Determining the cancer genome of individual patients will make these rather blunt tools sharper, and more effective, kinder drugs are actively sought. It still remains the tenet of cancer molecular biologists that understanding these systems is the first step in this complex endeavour and there is optimism in this community that much more can be done to achieve this goal.

Conflict of interest statement

None declared.