S4. Cancer Molecular Targeting: Can the Medicine of Today Become the Magic of Tomorrow

T.W. Mak

Princess Margaret Hospital, Campbell Family Institute, Toronto, Ontario, Canada

Over the past decade, a great deal of effort has been dedicated to identifying the genetic defects underlying cancers and developing drugs aimed at targeting the molecular pathways responsible for those defects. There is tremendous hope and faith in the ability of scientists to successfully isolate the most important targets, and great confidence that the biopharmaceutical industry will produce chemotherapeutic agents effective against these targets. In this presentation, I will discuss the rationale for this enthusiasm and provide some insight into progress in this area. Tumours arise and metastasize because of the cumulative effects of multiple mutations on key genes. Oncogenes undergo mutations that cause them to become active when they shouldn't, and tumor suppressor genes (TSGs) sustain damaging alterations that obliterate their protective functions. TSGs include genes that normally regulate cell growth and the cell cycle, control cellular differentiation, participate in DNA repair, and govern pathways leading to programmed cell death or survival. Molecular oncologists seeking mechanistically-based drugs for cancer treatment originally concentrated on the development of agents that block cell cycle progression and thus cancer cell growth. However, an emerging concept in cancer research today is that cancer therapeutics should be targeting cell survival genes that prevent cancer cells from dying. Three major intracellular signaling pathways involving a plethora of known and unknown genes promote cell survival. I will discuss some of the work in our laboratory that has dissected these signaling pathways and has pinpointed the activation of cell survival or anti-apoptotic genes as prime targets for the new generation of molecular cancer therapeutics.