In health and in disease: aberrant and normal functions of protein kinases

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Gruppens kerneforskningsområder

Protein kinases are enzymes that regulate many cellular functions, notably cell division, cellular differentiation, development and morphogenesis. Deregulated protein kinases activity is a frequent cause of disease, in particular cancer wherein these enzymes control cell growth, movement and death. Our research group employs in vitro (human cell lines) and in vivo (transgenic mice) model systems and focuses on the identification of the regulatory role of specific protein kinases in cardiac development. We also focus on protein kinases' aberrant role in the aetiology of specific types of cancer and explore a number of strategies for the induction of cell death. These studies combined with experiments with animal models constitute a large part of the preclinical investigations that we carry out in collaboration with national and international research groups.

Er du interesseret i at skrive projekt i gruppen, så kontakt : bag@bmb.sdu.dk

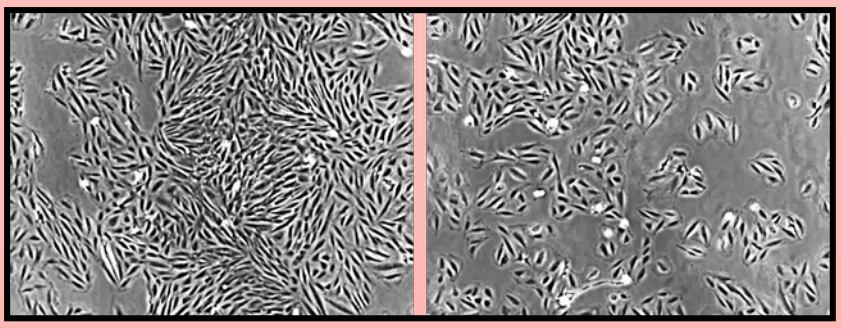

Fig. 1. Cardiomyoblasts expressing protein kinase CK2 (left) or lacking its expression (right). Note the difference in cell density which is not caused by induction of cell death but rather a difficulty to proliferate.

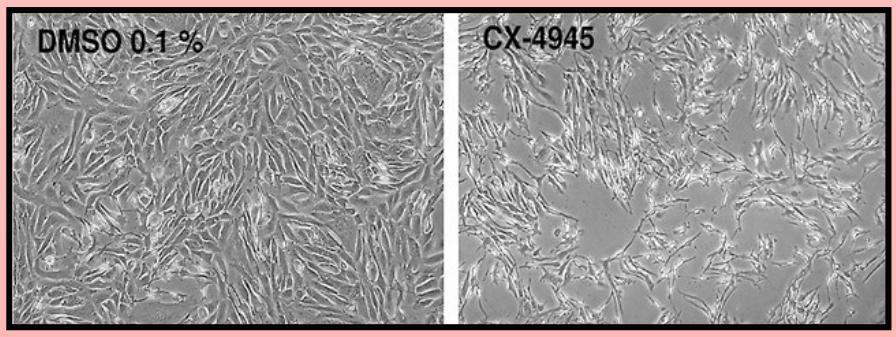

Fig. 2. Renal Cell Carcinoma cells left untreated (left) or treated with a protein kinase inhibitor (right). Note the severe effect on cell survival on those cells incubated with the drug.

Projekter	Beskrivelse
Protein kinase-mediated signalling networks involved in the regulation of cardiac cells' development and function	The mechanisms regulating the expression of cardiac specific genes remain not completely understood. In mammals, the essential role of CK2α in morphogenetic processes during embryonic development is reflected in the non-viable phenotype obtained upon gene deletion in mice. CK2α gene-deficient mice die at embryonic day E.11 and display abnormal heart tube. To date, it is unknown what fundamental cellular processes are responsible for the observed embryonic lethality. We are currently investigating a number of transcription factors regulated by CK2 in order to demonstrate that this enzyme functions in multiple aspects of heart development directing cardiac cells maturation and growth (Fig. 1).
Molecular mechanisms controlling cholesterogenic gene expression	Coronary heart disease is the leading cause of mortality in developed countries. Large studies have shown that persistent high levels of circulating cholesterol are strongly associated with the risk of developing coronary heart disease. Strategies adopted in order to lower hypercholesterolemia include pharmacological treatment. In this respect, statins are a class of drugs often prescribed in order to lower plasma cholesterol levels. However, there are groups of patients that do not tolerate this drug. We are currently investigating molecular mechanisms controlling the expression of cholesterogenic genes in order to set up alternative therapeutic strategies with the hope of enabling more patients to achieve recommended cholesterol levels in the future.
Molecular aberrations in renal cll carcinoma: identification of novel strategies for targeted cancer therapy	Renal cell carcinoma (RCC) accounts for approximately 85% of all types of renal cancer. RCC is characterized by exceptionally high resistance to radiation and chemotherapy, which can be explained by the typical genetic hallmark and high levels of expression of multidrug transporters. We have recently obtained evidence showing that inhibition of specific protein kinases induce significant cytotoxicity in renal cancer cells suggesting that blocking their activity may represent a new option to overcome resistance to current treatment of RCC. Their characterization might contribute to the development of more effective pharmacological approaches for the treatment of this fatal disease (Figure 2).