

Wednesday, 15th May, 11.00 pm, Seminar Room

Host: Dr. Jesús Ruiz-Cabello

p38 γ is essential for cell cycle progression and liver tumorigenesis

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The cell cycle is a tightly regulated process that is controlled by the conserved cyclin-dependent kinase (CDK)–cyclin protein complex¹. However, control of the G₀ to G₁ transition is not completely understood. Here we demonstrate that p38 MAPK gamma (p38g) acts as a CDK-like kinase and thus cooperates with CDKs, regulating entry into the cell cycle. p38g shares high sequence homology, inhibition sensitivity and substrate specificity with CDK family members. In hepatocytes, p38g induces proliferation after partial hepatectomy by promoting the phosphorylation of retinoblastoma tumour suppressor protein at known CDK target residues. Lack of p38g or treatment with the p38g inhibitor pirfenidone protects against the chemically induced formation of liver tumours. Furthermore, biopsies of human hepatocellular carcinoma show high p38g expression, suggesting that p38g could be a therapeutic target in the treatment of this disease.