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# IRES-dependent regulation of FGF-2 mRNA translation in pathophysiological conditions in the mouse

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## Abstract

The mRNA coding for FGF-2 (fibroblast growth factor 2), a major angiogenic factor, is translated by an IRES (internal ribosome entry site)-dependent mechanism. We have studied the role of the IRES in the regulation of FGF-2 expression *in vivo*, under pathophysiological conditions, by creating transgenic mice lines expressing bioluminescent bicistronic transgenes. Analysis of FGF-2 IRES activity indicates strong tissue specificity in adult brain and testis, suggesting a role of the IRES in the activation of FGF-2 expression in testis maturation and brain function. We have explored translational control of FGF-2 mRNA under diabetic hyperglycaemic conditions, as FGF-2 is implied in diabetes-related vascular complications. FGF-2 IRES is specifically activated in the aorta wall in streptozotocin-induced diabetic mice, in correlation with increased expression of endogenous FGF-2. Thus, under hyperglycaemic conditions, where cap-dependent translation is blocked, IRES activation participates in FGF-2 overexpression, which is one of the keys of diabetes-linked atherosclerosis aggravation. IRES activation under such pathophysiological conditions may involve ITAFs (IRES *trans*-acting factors), such as p53 or hnRNP A1 (heterogeneous nuclear ribonucleoprotein A1), recently identified as inhibitory or activatory ITAFs respectively for FGF-2 IRES.