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

I.G. Gonzalez-Herrera*, L. Prado-Lourenco*†, S. Teshima-Kondo‡, K. Kondo‡, F. Cabon§, J.-F. Arnal*, F. Bayard* and A.-C. Prats*₁

*Institut National de la Santé et de la Recherche Médicale U589, "Hormones, facteurs de croissance et physiopathologie vasculaire", Institut Louis Bugnard, IFR31, CHU Rangueil, Bâtiment L3, Avenue Jean Poulhes, BP 84225, 31432 Toulouse Cedex 4, France, †MilleGen, Prologue Biotech, Rue Pierre et Marie Curie, BP700, 31319 Labège Cedex, France, ‡Department of Nutrition, School of Medicine, University of Tokushima, 3-18-15 Kuramoto-cho, Tokushima 770-8503, Japan, and §Laboratoire "Oncogénèse, Différenciation et Transduction du Signal", CNRS UPR 9079, Institut Andre Lwoff, 7 rue Guy Moquet, 94800 Villejuif, France

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.