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Glucocorticoids, growth factors and Epstein-Barr virus (1987-1991) Departement de Biochimie I (Head Prof. J. P. Ebel) Institut de Biologie Moléculaire et Cellulaire du CNRS, Strasbourg, France

During my PhD (1987-1991) at the Biochemistry Department IBMC, Strasbourg (head: Pr. J.-P. Ebel; team: Dr G. Beck), I studied the effect of glucocorticoids and growth factors on the induction of the Epstein Barr virus early genes in human Burkitt lymphoma cell lines. I demonstrated that glucocorticoids are able to induce early antigen synthesis via glucocorticoid responsive elements present in the viral genome. These elements were identified and characterized. The presence of such elements may explain reactivation of the viral production under stress conditions.

Transfert RNA selenocystein ($tRNA^{Sec}$) gene transcription by Staf (1992-1999) UPR 9002, Institut de Biologie Moléculaire et Cellulaire du CNRS, Strasbourg, France

After my PhD defense, I joined the group of Prof. P. Carbon and Dr A. Krol, at UPR 9002 (head: Pr B. Ehresmann) at IBMC Strasbourg. Beginning as a post-doc (1992-1995), I integrated Inserm, the National Institut of Health of France, as research associate in 1995.

Selenium is an essential micronutrient for man and animals. The role of selenium has been largely attributed to its presence in selenoproteins as the 21st amino acid selenocysteine (Sec). Sec is encoded by a UGA codon in the selenoprotein mRNA. Sec incorporation in the protein sequence is mediated by the $tRNA^{Sec}$, a tRNA recognizing the UGA codon as a Sec codon in a specific structural context. $tRNA^{Sec}$ presents unique features of structure and transcription mechanism. In contrast to all the other tRNAs, $tRNA^{Sec}$ transcription is similar to the U6 small nucleolar RNA. This means that RNA polymerase III transcription is directed via external promoter elements and an activator element. We characterized the $tRNA^{Sec}$ promoter and activator elements and using an expression library screening we isolated the transcription factor interacting specifically with the activator element. The factor was called Staf for Selenocysteine tRNA gene Transcription Activating Factor. Using Xenopus oocytes intranuclear injections we demonstrated that Staf activates specifically the $tRNA^{Sec}$ but also many other genes transcribed by RNA polymerase II and III. This activation factor presents the particularity to contain two distinct transcription activation domains, that I fine-mapped and characterized as domains specialized in RNA polymerase III and RNA polymerase II transcription respectively.

Early steps in Hepatitis C viral life cycle and HCV vaccines (2000-2005), Inserm unit U544 Institute of Virology of Strasbourg, University of Strasbourg, France

In 2000, I joined Dr M.P. Kieny's team at the U544 of the Institut de Virologie, Strasbourg, France, as a "young team leader" (Label Jeune équipe, lauréat du prix "Jeune Chercheur" de la Fondation BNP-Paribas).

HCV is a major cause of hepatitis in the world. The majority of HCV-infected individuals develop chronic infection, which may progress to liver cirrhosis and hepatocellular carcinoma. Preventive modalities are absent and the current antiviral treatment is limited by resistance, toxicity and high costs. Our research was focused on the translation and replication steps of the hepatitis C virus (HCV) life cycle. First, we deciphered the structural features of the 3' end of the HCV genome. Our objective, was next to examine all potential interactions between HCV non structural (NS) proteins which could result in the formation of

the replication complex. We identified several viral interacting partners by in vitro and ex vivo coimmunoprecipitation experiments in adenovirus-infected Huh-7 cells allowing the expression of HCV NS proteins, and, finally, by using the yeast two-hybrid system. In addition, by confocal laser scanning microscopy, NS proteins were clearly shown to colocalize when expressed together in Huh-7 cells. We have thus been able to demonstrate the existence of a complex network of interactions involving all six NS proteins. Other studies were focused on regulation of translation.

During this period, we were active partners of the FP6 HCV European networks HepCVacc and HepCVax (2000-2006). Our task was to deliver, to our partner teams, vaccine candidates based on adenoviral and vaccinia (MVA) engineered viruses encoding most of the viral proteins alone or in combination.

Virus-host interactions and liver diseases (since 2006), Inserm unit U748/U1110 Institute of Virology of Strasbourg, University of Strasbourg, France

After the departure of Dr M.P Kieny for the World Health Organization (Geneva, Switzerland) Prof. T. Baumert became in 2006 the head of Inserm U1110 at the Institut de Virologie, Strasbourg. Research at Inserm U748 is focused on virus-host interactions and liver diseases. I pursued my research as a group leader focusing on HCV-host interactions. Aiming at the identification of novel targets for preventive and therapeutic strategies against HCV-induced liver disease, we focus on the characterization of virus host-interactions and the pathogenesis of HCV infection during the late steps of the HCV life cycle. I'm especially interested in the relationship between HCV and the cellular lipids and lipoproteins as well as the regulation HCV IRES driven translation. Since 2011 I'm Research Director at Inserm and deputy head of Inserm unit U1110.

My research at U1110 is focused on the relationship between hepatitis C virus and lipid metabolism host factors at various steps of the viral cycle as well as the regulation of HCV IRES driven translation.