

## 6- Appendix

### 6.1- Abbreviations

°C	degree Celcius
µg	microgram
2'5'OAS	2'5'oligoadenylate synthetase
Ad5	human adenovirus type 5
Adbiluc	adenoviral vector containing the bidirectional tet-regulated promoter P <sub>bi-1</sub> fused to luciferase gene
AdGH1.3	adenoviral vector containing the 1.3 overlenght HBV genome and the GFP gene under the control of CMV promoter
ALT	alanine transaminase (GTP)
cccDNA	covalently closed circular DNA
CMV	Cytomegalovirus
CTL	cytotoxic T Lymphocytes
DHBV	Duck Hepatitis B Virus
DMSO	dimethyl sulfoxide
dNTP	deoxynucleotide triphosphate
dox	doxycycline
E. coli	Escherichia coli
ELISA	enzyme-linked immunosorbent assay
FCS	fetal bovine serum
fig	figure
fmol	fetomole
GAPDH	glyceraldehyde-3-phosphate
GFP	green fluoresent protein
HBeAg	antigen of e protein as precursor of core protein of HBV
HBsAg	antigen of S envelope protein of HBV
HBV	human Hepatitis B Virus
HCV	human Hepatitis C Virus
HD	Helper-dependant adenoviral vector
HIV	Human Immunodeficiency Virus
i.p.	intraperitineous
I.U.	international unit
i.v.	intravenuous
IFN	interferon
IL	interleukin
IP10	CXC chemokine IFN $\gamma$ -inducible protein-10 (IP-10/CXCL10)
kb	kilobase
kDa	kilo Dalton
LCMV	lymphocytic choriomeningitis
LDH	lactate deshydrogenase
MCMV	mouse cytomegalovirus
MHC	major histocompatibility complex
mIFN	mouse interferon
ml	milliliter

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mM	millimolar
moi	multiplicity of infection
MVL	mouse
NK	natural killer cells
NKT	natural killer T cell
nm	nanometer
NPC	non-parenchymal cells
OD	optical density
OFR	open reading frame
p.i.	post infection
P <sub>CMV</sub>	major immediate-early promoter of cytomegalovirus
PCR	polymerase chain reaction
PDH	primary duck hepatocytes
PHH	primary human hepatocytes
PKR	double-stranded RNA-activated protein kinase
PMH	primary mouse hepatocytes
P <sub>TTR</sub>	promoter and enhancer element of transthyretin gene
rpm	rotation per minute
rtTA	reverse tetracycline-dependent transactivator
tet	tetracycline
TNF $\alpha$	tumor necrosis factor alpha
tTA	tetracycline-dependent transactivator
v.p.	viral particle
WHV	Woodchuck Hepatitis Virus
wIFN	woodchuck interferon

## 6.2- References

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## 6.3- Curriculum vitae

### *Personal data*

**Surname:** Dumortier  
**Given names:** Jérôme, Roland, Jean-Pierre, Bernadin  
**Date of birth:** 1970/ 05/ 20  
**Place of birth:** Déville-les-Rouen , Seine-Maritime (76), France.  
**Nationality:** French



### *Education*

2000-2003 **Ph.D program**  
Center for Molecular Biology Heidelberg (ZMBH),  
Prof. Dr. H. Schaller and PD Dr. med. U. Protzer  
University of Heidelberg (Germany)

1998-1999 **Diploma thesis**  
Molecular Genetics, Virology  
Institute for Med. Microbiology and Hygiene,  
Prof. Dr. R. E. Streeck and Prof. Dr. R. Prange  
University of Mainz (Germany)

1994-1997 **M.Sc. (Diplomprüfung) in Biology**  
Microbiology, Molecular Genetics, Plant Biology and Computer programming  
University of Mainz (Germany)

1990 **B.Sc. (D.U.T.), Applied Biology,**  
Food industry and Biochemistry  
Institute for Technology (I.U.T.)  
University of Caen (France)

1988 **High School Diploma (Baccalauréat)**  
mathematics and natural sciences  
Rouen (France)

***Professional Experiences***

- 2001-2003 **Research Worker**  
 Institute for Hygiene, Department of Virology,  
 University of Heidelberg (Germany)  
 Prof. Dr. med. H.G. Kräusslich and PD Dr. med. U. Protzer  
work: completion of research work for my thesis
- 1999-2001 **Research Worker**  
 ZMBH,  
 University of Heidelberg (Germany),  
 Prof. Dr. H. Schaller and PD Dr. med. U. Protzer  
work: research work for my thesis
- 1999 **Research Worker**  
 Department of laboratory Medicine, Transfusion Research Program,  
 University of California San Francisco (USA),  
 Prof. G.N. Vyas  
work: cloning of full-length genome of HBV variant extracted from  
 serum of seroconverted Alaska patients (2 months)
- 1999 **Research Worker**  
 Institute for Med. Microbiology and Hygiene,  
 University of Mainz (Germany)  
 Prof. Dr. R. E. Streeck and Prof. Dr. R. Prange  
work: mutagenesis on the cytosolic loop of the S protein and effects on  
 the assembly of Hepatitis B virus.
- 1999 **Transfusionszentrale**  
 Johannes-Gutenberg Klinikum Mainz (Germany)  
 student work at the laboratory for control, preparation and management  
 of blood-donations in hospital
- 1994-1996 **SuCrest GmbH**,  
 Hochheim/M (Germany)  
 student work in the Research and Development laboratory  
 Continuation of '90-'92 position on a part-time basis
- 1992-1994 **General Office Worker**  
**Union Laitière Normande Milchprodukte Germany GmbH**,  
 Bad Soden a. Ts. (Germany)  
 In connection with civil service, worked for a major french exporter of  
 dairy products in their office near Frankfurt, Germany  
job position: contact with clients, place orders and resolve problems of  
 transport and quality in cooperation with the marketing division of Paris
- 1990-1992 **Food Production Technician**  
**SuCrest GmbH**, Hochheim/M (Germany)  
 Work in Research and Development laboratory  
 Production of new cream coatings, caramels and for the chocolate and  
 confectionery industry. Manager: Mr. W. Schmedes
- 1990 **Analytical Institute of the cities Wuppertal and Solingen** (Germany),  
 Practical course (2 months): inspection of norms of food quality and  
 packaging in stores, analysis of soil and air samples.
- 1990 **Würzburger Hofbräu AG**, Würzburg (Germany),  
 Practical course with report (2 months): production of beer and control of  
 quality.

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## *Publications*

**Jérôme Dumortier**, Kai Schönig, Hermann Bujard and Ulrike Protzer; The Tet-system allows tight control and liver-specific gene expression *in vivo* following adenoviral gene transfer into mice; 2003; Mol. Therapy; (manuscript submitted).

M. Sprinzl, **J. Dumortier** and U. Protzer; Construction of recombinant adenoviruses that produce infectious HBV; 2003; R. Hamatke, J. Lau (eds.). Methods in Molecular Medicine. „Hepatitis B Virus Protocols“. The Human Press Inc., Totowa NJ; (in press).

**Jérôme Dumortier**, Andreas Limmer, Heike Oberwinkler and Ulrike Protzer; Cytokine Gene Therapy For Chronic Hepatitis B: Establishment in HBV Transgenic mice; 2002; Poster at the International Meeting for molecular Biology of Hepatitis B Viruses, Asilomar, California, USA.

**Jérôme Dumortier**, Kai Schönig, Hermann Bujard and Ulrike Protzer; Liver-specific and regulable gene expression following adenoviral gene transfer; 2002; Poster at the Conference for the germane society for Virology (GFV), Erlangen, Germany.

**Jérôme Dumortier**, Heike Oberwinkler, Andreas Limmer and Ulrike Protzer; Adenoviral Gene Transfer Of Cytokine Gene As Therapy To Repress Hepatitis B Virus Replication; 2001; Poster at the Gene Vector Production Network Conference (GVPN), Evry, France.

**Dumortier J.**, Ritter Th., Sprinzl M., Schaller H. and Protzer U.; Expression of Interferon Type I and II following Adenoviral Gene Transfer Inhibits Hepatitis B Virus Replication; 2001; Poster at the Conference for the germane society for Virology (GFV), Dresden, Germany.

**Jérôme Dumortier**, Heike Oberwinkler, Thomas Ritter, Andreas Limmer, Heinz Schaller and Ulrike Protzer; Expression of Interferon Gamma After Adenoviral Gene Transfer Inhibits HBV Replication; 2000; Poster at the International Meeting for molecular Biology of Hepatitis B Viruses, Paris, France.

Heike Löffler-Mary, **Jérôme Dumortier**, Carola Klentsch-Zimmer and Reinhild Prange; Hepatitis B Virus Assembly Is Sensitive to Changes in the Cytosolic S Loop of the Envelope Proteins; 2000; Virology 270: 358-367.

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C. Hartmann-Stühler, C.E. Lambert, A. Peichl, H. Löffler-Mary, **J. Dumortier**, M. Werr and R. Prange; Hepatitis B Virus morphogenesis: Structure requirements of the envelope proteins; 1999; Recent Res. Devel. Virol., 1: 251-268.

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I also wish to thank Prof. Dr. Valerie Bosch for accepting to be the second referee of this thesis and for closely following up on this work during presentations at internal seminars of her research group and the Virology Club of the University of Heidelberg

My hearty thanks go to PD Dr. med. Ulrike Protzer, the co-supervisor of this work, who introduced me into the practical aspects of adenovirus production and experiments with mice. Despite being very busy with her medical work in the diagnostic department, the preparation of her habilitation and her family, she still took time to support and advice me continuously in my work.

I also wish thank Prof. Dr. med. Hans-Georg Kräusslich for accepting to incorporate me into his Department thereby giving me the opportunity to continue the second part of this work in the new facilities of the Heidelberg Virology Department.

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I hereby confirm that this thesis entitled: “ Cytokine gene transfer by adenoviral vectors as a novel therapeutic option for hepatitis B virus infection” was entirely carried out by me and that all the materials used have been cited accordingly. This work has not been submitted to any other university.

Heidelberg, 10<sup>th</sup> February 2003

Jérôme Dumortier

## Jérôme's spirit for

Science



Sport



*the flying triplet*

from research group for HBV



Heidelbergman triathlon

2000: 8. position

2001: 5. position

2002: 2. position

