The anticancer potential of autonomous rodent paroviruses (PV) is supported by a large set of observations, including the dependence of their life-cycle on the proliferation and oncogenic transformation of host cells, their oncolytic and oncosuppressive effects in pre-clinical models, and their experimental infectiousness but excellent tolerance in humans. This has led the Unit to set itself as main challenge to bring PV to the forefront of cancer virotherapy. Work carried out in the Unit has contributed to optimising the production of PV and recombinant vector derivatives, unravelling their cytopathic effects, and assessing the impact of PV (vectors) on effector cells of the innate and acquired immune responses. The medical relevance of these achievements lies in the fact that PV multiplication is a limiting factor for tumour destruction, and that oncolysis and immunomodulation are the two major components of PV oncosuppression. The translational significance of our findings is apparent from the fact that they are considered satisfactory proof of concept by the national regulatory agency in charge of clinical trials. On the basis of this approval, the Unit is currently striving to meet the remaining prerequisites to launching a first phase I/II clinical trial in which the parvovirus H-1PV will be administered to malignant glioma patients. Concomitantly, we are developing second-generation modified, replication-competent PV and also new PV vectors and various parvomimetics endowed with an enhanced oncosuppressive capacity, in the hope of preparing further clinical evaluation of PV-based anticancer preparations.
Partnerships and collaborations
22 international collaborations from which resulted 33 joint publications.

Clinical and public health transfer
A clinical trial (phase I/II) is in preparation with the purpose of confirming the innocuity (and secondly, searching for first indications of efficacy) of the oncolytic parvovirus H-1 PV injected intratumorally to patients with malignant glioma. This clinical study will be carried out in the Neurosurgery Department of the University Hospital of Heidelberg.

The rationale for this approach and the virus production procedures have been presented to the German National Organism being responsible for the homologation of clinical trials, the Paul-Ehrlich Institute (PEI, Langen). Our project has been discussed in detail by a Consulting Committee, the conclusions of which can be read in an official document entitled “Advice on preparation of a clinical trial (phase I/IIA) on Oncolytic Glioma Therapy by Parvovirus H-1 PV”. The PEI considers that the preclinical data obtained by the Unit supply a sufficient proof of concept to justify conducting a clinical trial, and recommend the identification of approved platforms to carry out the production of H-1PV virus under GMP conditions as well as prescribed toxicology, pharmacology and quality tests.

Consequently, we endeavoured to look for the above-mentioned technological platforms on the one hand, and partners on the other hand, who are willing to finance the project. These efforts have benefited from the help of INSERM-Transfert/Cossec and the National Center for Tumor Diseases/Heidelberg. In this connection, it is noteworthy that the envisaged application is protected by a patent which was recently granted to us (US patent no. 7, 179, 456 B2 [2007]). This prospect has enabled us to identify the above-mentioned platforms and a sponsor who undertook to support the project. The Authorities of the DKFZ have assured us that the proposed trial was of priority for the Organism which approved a “Clinical Development Plan” defining the nature and timing of the different steps involved in the preparation, realization and control of the clinical trial.

Technology transfer
6 granted patents.

Key publications


Nüesch, J.P.F.et.al.

Ezrin-Radixin-Moesin family proteins are involved in parvovirus replication and spreading. J.Virol., 83, 5854-63.