

Saarbrücken, March 2004

### **German-Belgian Duo tests histones in leukemia**

The biotech companies SymbioTec GmbH, based in Saarbrücken, Germany, and Eurogentec S.A. from Liège, Belgium, signed a cooperation agreement in March 2004. Their common goal is the development of a novel histone-based cancer therapeutic.

SymbioTec's scientists have discovered over the past years that histones are an ancient component of the human innate immune defense. In particular, histone H1 recognizes tumor cells and pathogens due to their particular surface structures. Several histone molecules then aggregate to form a transmembrane tunnel, similar to the complement system's C-9 protein. The attacked target cells are lysed and die.

At present, all preclinical studies are completed, and the Saar scientists have started testing their human histone H1 for the first time in leukemia patients at the Saarland University Hospital in Homburg. The first clinical phase I Study is being conducted by professors Michael Pfreundschuh and Christoph Renner, Department of Internal Medicine I. Oncology Services Europa S.A.R.L. a Contract Research Organization based in Strasbourg who is specialized in oncology is in charge of the study management and the communication with the regulatory authorities. The protein quantities required are produced in fermenters of the Belgian company Eurogentec using recombinant E.coli strains. This company, founded in 1985, belongs to the very pioneers in European biotechnology and specializes, inter alia, in producing genetically engineered clinical test samples. In return, the agreement grants Eurogentec profit shares from licensing agreements, which SymbioTec will earn from the pharmaceutical use of histone H1 in the future.

Professor Michael Zeppezauer, SymbioTec's CEO, states: "Eurogentec is the perfect partner for us to realize our goals because of their tremendous experience in the production of therapeutic proteins". The cooperation agreement is the result of several years of a very productive collaboration. Thus, Eurogentec already produced histones in quantities required for research and development in GLP quality for SymbioTec's preclinical studies. Scientists and technicians of both companies have now succeeded in developing the process for GMP, and the yields have been optimized sufficiently so as to produce enough material for the clinical trial. In the future, further improvements of process control and purification are ongoing so that enough histone H1 will be provided for larger studies and market needs.

SymbioTec presently holds over 40 patents for medical use of histones. All studies done so far indicate that histone H1 may become the ideal therapeutic for leukemia, according to Professor Zeppezauer, who discovered as early as in the 1980's that histones are more than passive spools for the DNA molecule. "Histone H1 distributes in the body exceptionally well and penetrates the bone marrow better than other drugs, where it can attack leukemia cells directly at the source." In animal studies, histone H1 has already impressively proven its efficacy against human leukemias. However, SymbioTec experts do not consider the application of histones to be limited only to leukemias, although research has progressed furthest in this area in collaboration with Eurogentec. They foresee further applications of histones in cancers of the breast, skin and prostate, as well as sepsis and autoimmune diseases such as rheumatoid arthritis or Lupus erythematoses.