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Live attenuated *Listeria* as new delivery platform for anticancer agents

Our laboratory has built a platform for the selective delivery of anticancer agents to the tumor microenvironment (TME) using a live attenuated bacterium *Listeria monocytogenes*. We discovered that *Listeria* could infect and kill tumor cells through reactive oxygen species and selectively survives and multiplies in tumors and metastases but not in normal tissues because of the strong immune suppression in the TME that is absent in normal tissues. *Listeria* can infect tumor cells directly or through infection of myeloid-derived suppressor cells (MDSC), which are selectively attracted to the TME through cytokines and chemokines. Once at the tumor site, *Listeria* efficiently moves from MDSC into tumor cells through a mechanism specific for *Listeria*. This novel discovery opened doors for the development of complete new therapies particularly for non-curable metastatic cancers. We developed *Listeria*-¹⁸⁸Rhenium and *Listeria*-³²P. Both have been tested in preclinical models for biodistribution, efficacy and safety. These radioactive *Listeria* bacteria strongly reduced the growth of the pancreatic cancer at early and advanced stages in various mouse tumor models with practically no side effects. We also generated *Listeria*-based vaccines, expressing highly immunogenic “recall antigens” (RA) derived from tetanus toxoid (TT) protein, polio virus (PV) and measles virus (MV), which in combination with low doses of Gemcitabine, resulted in the reactivation of memory T cells to RA (generated during childhood vaccination and circulating in blood for life), now capable of killing *Listeria*-RA-infected tumor cells with help of Gemcitabine-reduced immune suppression. These results demonstrate the potential of *Listeria* as selective delivery platform for anticancer agents. Delivery of adjuvants, RNAs, apoptotic genes, small molecules by *Listeria* to the TME could be a promising next step in the fight against metastatic cancer.

Biography

Claudia Gravekamp is an Associate Professor in the Department of Microbiology and Immunology of the Albert Einstein College of Medicine in New York and a Member of the Albert Einstein Cancer Center. She has received her PhD in 1988 in the field of Tumor Immunology at the Erasmus University in Rotterdam, Netherlands. From 1987-1993, she has served as Head of the Laboratory for Leptospirosis at the Royal Tropical Institute in Amsterdam, Netherlands. In 1993, she started as a Research Fellow in Medicine at the Channing Laboratory of the Brigham and Women's Hospital, Harvard Medical School, USA and became an Instructor in Medicine until 1998. From 1998 to 2006, she was an Associate Member in the Institute for Drug Development of the Cancer Therapy and Research Center and an Assistant Professor at the University of Texas Health Science Center, in San Antonio, TX. In San Antonio she began to develop a program aimed at genetic vaccines for breast cancer. From 2006-2008, she was a Scientist at the California Pacific Medical Center Research Institute in San Francisco, CA. She has published 65 scientific articles, is ad-hoc Reviewer for various scientific journals and Reviewer on multiple NIH study sections.

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