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Characterisation of Adenovirus trans-complementation-mediated gene expression controlled by melanoma-specific TETP promoter

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Human adenoviruses (Ads) have substantial potential for clinical applications in cancer patients. Conditionally replicating adenoviruses (CRAds) include oncolytic adenoviruses in which expression of the immediate early viral transactivator protein E1A is controlled by a cancer cell-selective promoter. To enhance efficacy, CRAds are further armed to contain therapeutic genes. Due to size constraints of the capsid geometry, the capacity for packaging transgenes into Ads is, however, limited. To overcome this limitation, the employment of E1A-deleted replication-deficient viruses carrying therapeutic genes in combination with replication-competent CRAd vectors expressing E1A *in trans* has been proposed. Most trans-complementing studies involved transgene expressions from strong ubiquitous promoters, and thereby relied entirely on the cancer cell specificity of the CRAd vector. We tested the trans-complementation of a CRAd and a replication-deficient transgene vector containing the same cancer cell-selective promoter. We generated two vectors expressing IL-2 and CD40L from a bicistronic expression cassette under the control of the melanoma/melanocyte-specific tyrosinase enhancer tyrosinase promoter (TETP). These vectors gave rise to tightly controlled melanoma-specific transgene expression levels but the cancer cell-selective TETP did not give the expected enforceable transgene expression typically achieved in the Ad trans-complementing system. Reasons for this could include virus-mediated down regulation of limiting transcription factors, and/or competition for such factors by different promoters and warrants further investigations.

Biography

Dr. med. A. Curioni-Fontecedro has completed her medical studies in 2004 in the University of Rome Campus Biomedico and in 2005 received her MD title from the University of Zurich and the University of Rome Campus Biomedico.

She was scientific physician in the Laboratory of Tumor immunology of the University Hospital of Zurich from 2005 to 2007.

Since 2007 she is physician in the Department of Oncology and Internal Medicine, leading and participating to research and clinical studies in the area of tumor immunology.