

PRECLINICAL EVALUATION OF A NEW THERAPEUTIC APPROACH: DNA VACCINATION PROTECTS AGAINST CHEMICALLY INDUCED ORAL SQUAMOUS CELL CARCINOMAS

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Immunotherapy is more and more considered as an important approach in cancer therapy, and big efforts are directed toward the setting of anticancer vaccine. Fundamental to this goal is the choice of the appropriate target. An increased Her-2/*neu* gene copy number and/or excess cell membrane expression of p185 is a frequent event in oral squamous cell carcinoma (OSCC), the most common type of oral neoplasm. We already demonstrated that DNA vaccination against the tumor antigen Her-2 protects against squamous cell carcinoma progression in a transplantable *in vivo* model. We therefore decided to apply this approach to a model closer to the human situation, represented by the chemically induced OSCC. We can induce OSCC in hamster cheek pouches by painting them trice a week with dimethylbenzanthracene (DMBA). We first tracked, by immunohistochemical analysis, the expression of Her-2 all along the chemical carcinogenesis process to determine its onset, and we found out that it appears already at the fourth week after induction began and persists all along the experimental period. We then set the vaccination protocols (beginning three weeks before chemical induction and boosting animals every second week) and injected DNA plasmids coding for the extracellular and transmembrane domains of rat Her-2 receptor (EC-TM plasmids) or, in control animals, the empty plasmid. Vaccination was improved by helping DNA entrance in target cells through electroporation. This technique designates the use of short high-voltage pulses to overcome the barrier of the cell membrane. Animals were observed all along the experimental period and checked weekly for counting and measuring preneoplastic and neoplastic lesions. Data will beshown demonstrating that DNA vaccination against Her-2 significantly delays the onset of preneoplastic lesions, it lowers the number of preneoplastic (p=0.045 at 9-10 weeks, p=0.008 at 11-12 weeks) and of exophytic lesions (p=0.007 at 14 weeks) per animal. We also investigated the different cellular and molecular mechanisms potentially involved in tumor growth inhibition. Our observations provide important evidence for the potential use of Her-2 DNA vaccination in the treatment of human oral cancer, especially in the prevention of the progression of diffuse lesions and postoperative recurrences.