

DEVELOPMENT OF THE DNA PLASMID BASED GENETIC VACCINES VECTORS, WHICH USE SEGREGATION AND PARTITIONING FUNCTION OF THE BOVINE PAPILLOMAVIRUS TYPE 1

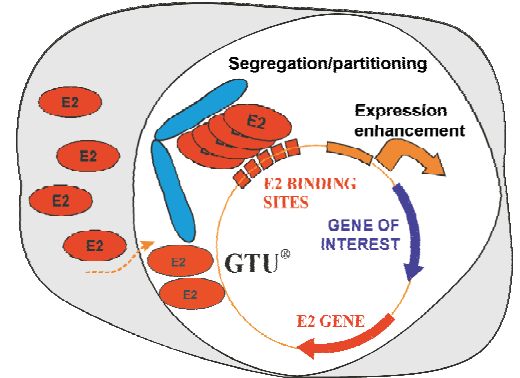


FIT BIOTECH

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PRINCIPLES OF GTU[®]



The E2 protein with the multimeric E2 binding sites present in the GTU[®] vector provide both chromatin mediated segregation/partitioning function and activation of the antigen expression.

Background:

We developed a novel DNA vaccine vector technology called Gene Transport Unit (GTU), which uses the segregation/partitioning function of the Bovine papillomavirus (BPV1). Two elements were added to a plasmid already loaded with a novel bacterial selection marker and with an optimized expression cassette for antigens: 1) the BPV1 E2 protein expression cassette and 2) multimeric binding sites of the E2 protein. Expression of the gene of interest and E2 was directed either by ubiquitous or tissue-specific promoters for unrestricted or cell type-specific expression. The expression properties of GTU[®] vectors in different tissues of mice, swine and non-human primates were analyzed using gene gun, jet-injection, IM and ID needle injection delivery alone and in combination with electroporation.

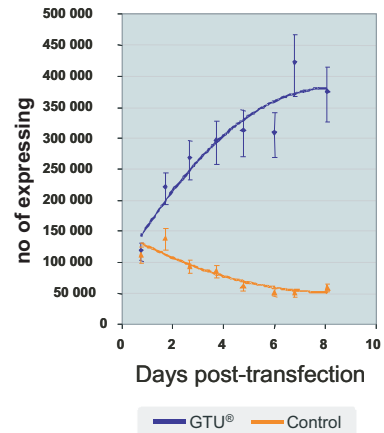
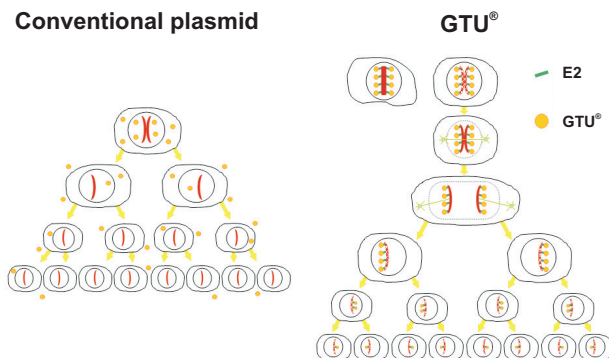
Results:

Two novel features were provided by the E2 protein and multimeric E2 binding sites. First, the viral segregation/partitioning function increased the number of antigen-positive cells as a result of division of cells, therefore engaging a larger number of cells for expression of the antigen as shown in macaque and swine skin. Second, transcriptional activation provided by E2 and E2 binding sites increased expression of the antigen at least 10-fold compared to the regular plasmids in the muscle. The GTU vectors carry the novel auxotrophic selection marker. Complete cGMP technology for large-scale production has been developed. The DNA vaccine against HIV1/AIDS based on GTU technology has been successfully tested in five clinical trials with an outstanding safety and efficacy profile.

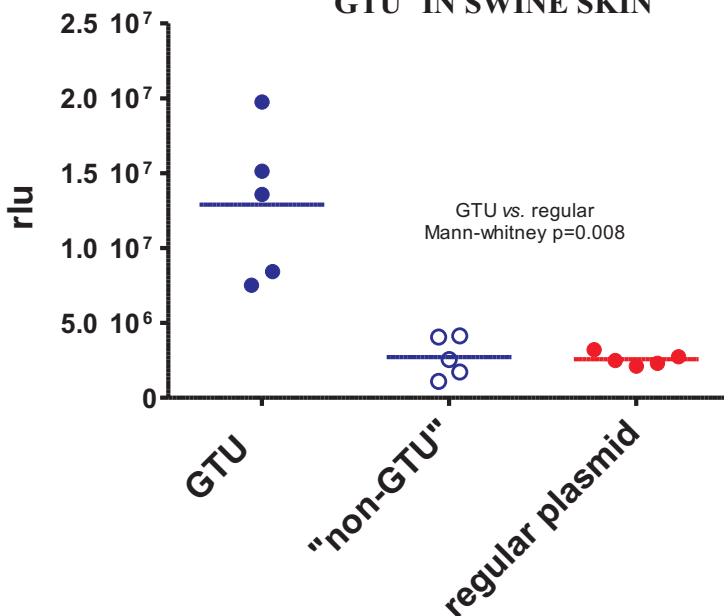
Conclusions:

GTU[®]-based vectors were safe and efficacious in inducing both humoral and cell-mediated immune responses against HIV1 in humans.

SPREADING OF GTU[®] IN PROLIFERATING CELLS



SUPERIOR EXPRESSION OF GTU[®] IN SWINE SKIN



SUPERIOR EXPRESSION OF GTU[®] IN MOUSE SKELETAL MUSCLE

