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PBMCs transfected with RNActive stimulate specific T-cells R Teufel¹, J-P Carralot^{1,2}, B Scheel¹, I Hörr¹ and Steve Pascolo*¹

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Vaccination with messenger RNA (mRNA)-transfected dendritic cells (DCs) is a very potent and versatile strategy for immune intervention. It has recently been reported to trigger specific T-cell responses and clinical benefit when used as anti-tumor vaccine in cancer patients. Towards the improvement of this promising technology, most researchers studied the optimal transfection methods, maturation signals and application sites of DCs. On the contrary, we focused our research on the improvement of the other active component of this vaccine that is mRNA. We studied the stability and efficiency of translation of different mRNA designed to have improved futures. Through this work, we could develop an optimal mRNA vector called RNActive™ which enhances the efficiency of mRNA-based immune stimulations. Besides, we tested the possibility of replacing DCs by some other immune cells as a recipient of the mRNA. We found that under certain conditions, mRNA can be transfected in PBMCs preparations. The expression of relevant antigens through this mRNA transfection technology results in the presentation of MHC-associated epitopes as demonstrated by the stimulation of antigen-specific T-cells. This method is a bloodsaving replacement of mRNA-transfected DCs. It is useful especially in the context of immunomonitoring: a small amount of PBMCs is enough to generate mRNA-transfected autologous cells. These cells can be used as targets in *in vitro* assays where the T-cell response that developed in vaccinated patients is being studied. Thus, our work on mRNA-technologies offers new tools to improve and study the triggering of immune responses using mRNAbased vaccines.