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Synthetic mRNAs as optimized tools for stem cell generation and for manipulating cellular phenotypes

Availability of high quality synthetic mRNAs (syn-mRNAs) has enabled progress in their applications. Tremendous, rapidly growing interest of notable private investors and BIG PHARMA has created a novel multi-hundred-million € business; a rare situation where two German enterprises are among the three top players in the field. AmpTec recognizes its obligation to support new players by providing customized, high quality mRNA products. Important structural features, alternative technical options for high-amount, high-quality mRNA synthesis and GMP-compliant manufacturing and quality requirements are presented. Requirements in the application of mRNA-mediated manipulation of cells are presented; mRNA-directed expression of antigens in dendritic cells for vaccination projects in oncogenesis, infectious disease and allergy prevention; reprogramming of human fibroblasts to induced pluripotent stem cells with their subsequent differentiation to the desired cell type; applications in gene therapy. In a recent overview, applications and corresponding syn-mRNA quality requirements were presented. Syn-mRNAs can be generated by *in vitro* transcription (IVT) from defined templates containing the synthetic gene of interest. Synthetic genes are provided as plasmid clones by commercial suppliers like Eurofins Genomics. In principle, linearised plasmids (with a restriction enzyme) can be used directly as templates in IVT reactions, however, this procedure is hampered by several disadvantages: Incomplete plasmid cleavage results in poor reproducibility due to variable amounts of very long and undefined background transcripts; high amounts of plasmid DNA introduce undesired bacterial components with possible interference in the intended cellular applications. Furthermore, optimal mRNA activity depends on a very long, unmasked poly-A tail. A good tail includes about 120 A nucleotides, but this hompolymeric repeat sequence is prone to random deletions during propagation in bacterial cells. We developed an alternative procedure with well defined PCR products as IVT-templates. The approach with example results will be presented. We will also present a detailed list of quality requirements for synthetic mRNAs in this application field. Problems observed in IVT-based mRNA synthesis are presented, combined with problem solutions.

Biography

Guido Krupp (PhD) is the CEO and President of AmpTec GmbH. In 1981, he received his PhD degree from Würzburg University & Max-Planck-Institute Martinsried. From 1983 to 1987, he was post-doc at Yale University. From 1987 to 2002, he served as research group Leader at Kiel University. He is the Founder of Artus GmbH (1998) & AmpTec GmbH (2005) & KSK Diagnostics GmbH (2015). His research interests include nucleic acid technology with focus on RNA, plant pathogens (viroids), ribozymes and telomerase. He has published more than 60 publications, editor of Ribozyme Biochemistry & Biotechnology, and of Telomeres, Telomerases & Cancer and Editorial Board Member of Biotechnology Annual Review.

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