Filip Lhota: Study of alternatively spliced variants of estrogen receptor alpha in breast cancer cell lines

Abstract:

Estrogen receptor α (ER-α) is a transcription factor responsible for mediation of the activities of its natural ligand 17-β-estradiol (E2), the hormone that together with progesterone belongs to the key regulators of mammary epithelial as well as breast cancer cells proliferation. Except to the major gene product consisting of all eight coding exons of ER-α, numerous qualitatively and quantitatively different spliced variants originated from primary transcript by activity of alternative splicing is expressed. Despite that some of these spliced variants have been functionally characterized, their precise role on final ER-α cellular activity remains to be elucidated. The functional characterization of individual alternative forms of ER-α and description of its participation on the overall ER-α activity is important for our understanding of their biogenesis and is also critical for the delineation of molecular bases for ER-α regulation during anti cancer chemotherapy.

This work aimed to study the influence of alternatively spliced ER-α variants on the growth characteristics of clones constructed from stable mammary tissue cell lines in regulation to cultivation conditions and cellular stimulation by E2 or tamoxifen. The model systems consisting of the stable transfectants with modified expression of alternatively spliced variant ER-αΔ7 was derived from ER-α negative MDA-MB-231 and ER-α positive MCF-7 cell lineages. The analysis of the growth characteristics in MDA-MB-231 expressing this variant shows that ER-αΔ7 was not capable of reintroduction of estrogen responsibility in these cells, whereas, the down-regulation of ER-αΔ7 in MCF-7 indicates that this variant contributed to the ER-α mediated signaling activities in both genomic and non-genomic pathways.