Developing nanotechnology based cancer therapeutics: RNA interference as a powerfull tool in gene silencing for p53

Ioana Berindan Neagoe1,2, Cornelia Braicu1, O.Balacescu1, Oana Tudoran1, Loredana Balacescu1,

Claudia Burz2, T.Kaucsar2, Roxana Redis2, V.Cristea2, Al.Irimie1,2

1 – Institute of Oncology Ion Chiricuta Cluj Napoca Romania

2 – University of Medicine and Pharmacy Iuliu Hatieganu Cluj Napoca Romania

Discovered only in the last ten years, RNA interference is a powerful tool that can be used to silence any gene of interest in many biological systems. To date, this technology has been used largely for research applications, involving cells grown in the laboratory or model organisms, as well as new therapeutics for cancer. Multi-disciplinary teams are involved to develop this technology forward so that it can be used as soon as possible to inhibit the function of cancer genes for cancer therapy.Our goal is to develop improved delivery methods such that RNAi molecules that can be given with less toxicity and more efficient in cancer patients. Again, targeting the RNAi molecules selectively only to cancer cells will likely be required to achieve the desired therapeutic results. Similar approaches are being developed for delivering therapeutic DNA molecules to cancer cells *in vivo*, including to replace the function of mutated tumor suppressor genes like p53.

p53 gene, discovered almost 35 years ago, keeps the main role in cell cycle control, apoptosis pathways and transcription. *p53* gene is found mutated in more than 50% of all human cancers in different locations.Many structures from viral to non viral were designed to incorporate and deliver in appropriate conditions, forms of *p53* gene or its transcripts, systemically, to target tumor cells and to eliminate them through apoptosis or to restore the normal tumor suppressor gene role.Each delivery system presents advantages and low performance in relation to immune system recognition and acceptance.One of the major discoveries in the last years, silencing of RNA, represents a powerful tool for inhibiting post transcriptional control of gene expression. According to several studies, the RNA silencing technology for p53 transcripts together with other carriers or transporters at nano level for *p53* gene can be used for creating new therapeutic models. RNA interference for p53 uses different ds (double strand) molecules like short interfering RNA and despite the difficulty of introducing them into mammalian cells due to immune system response it can be exploited into therapy.

Our study was focused in different types of human cancers, looking for inhibition by RNA interference og mutant p53 gene expression and implicitelly the restoration of the wild type p53 model as apoptotic feature of a dying cell.

Key words: nanotechnologies, apoptosis, cancer, p53, restoration, RNA interference, transcription