O410
1-hour Oral Session
Vaccines in the pipeline: far and close

Streptococcus pyogenes M protein mutant strain as live vaccine for cancer treatment

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Background: The search of different live bacterial or viral organisms which can be used as tools for the treatment of malignant tumors is one of the most interesting fields contemporary microbiology (Ascierto ML and all). *Straptococcus pyogenes* (GAS) was among the first bacterial species that has a potential to reduce and even cure cancer. In the present study we were investigating these mechanisms employing two different models: *in vitro* tissue culture and *in vivo* murine model. Anti-cancer effects of M39 GAS and it's emm^- mutant was evaluated in both models. M protein in GAS is one of the most important antiphagocytic protein, which was inactivated after the inserting the antibiotic resistant plasmid in the emm gene.

Material/methods: Two types of murine tumor cell lines: hepatoma 22a and sarcoma 37 were used in this study. *In vitro* experiments included testing of phagocytic and cytotoxic activity of the wild strain and it's emm^- mutant on the tumor cell lines. Cytotoxic activity was constantly monitored by ExCelligence ™ apparatus in 5% of CO_2. For the *in vivo* experiments hepatoma 22a and sarcoma 37 were induced in mice by subcutaneous injection and then treated by intra-tumoral injections of streptococci. Multiplications of streptococci in the tumor and spleen of mice was evaluated at different time points of the experiment.

Results: Phagocytic index and phagocytic number was much higher in emm- mutant strain comparing to the wild type strain. Both wild strain and emm- mutant showed high cytotoxic activity by usage of different methods, but emm- mutant strain degraded the tumor cells without further growth, when after using a wild strain we noticed the regrowth of the cell culture. In case of co- cultivation of both GAS strains with the tumor cells separated by the filter membrane only emm-mutant in was able destroyed the monolayer.

In both hepatoma and sarcoma models mice treated by emm- mutant strain showed significant repression of tumor growth in comparison with the wild type GAS strain.

Bacteriological study of streptococci in the tumor affected animals revealed that GAS was able to multiply inside the tumor of mice tumors for at least 10 days without significant reduction of the titer. In rare occasions few streptococcus were determined in the spleens of treated animals.

Conclusions: In all the experiments GAS strain with inactivated emm gene performed significantly better anti-tumor activity in comparison with the original GAS strain. We can suggest that the effects described can be explained by activation of the innate immune system that is focused on fighting pathogenic bacteria and by the direct contact with tumor cells and anti-tumoral cytotoxic factors exhaled by GAS.