A possible role of the hERG K^+ channel on DNA damage response

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Some voltage dependent K^+ channels, as those of the KCNH family Kv10.1 (eag) and Kv11.1 (hERG), can play an important role on processes like cell proliferation and/or tumour progression, conferring sometimes selective advantages to tumour cells. These effects can be related to the ability of those entities to impact the electrophysiological cell properties, but may also depend on some "non-canonical" properties of the protein, unrelated to its function as a conductive ionic channel.

The **h**uman ***e**ther-a-go-go*-**r**elated **g**ene (hERG) channel can be located not only at the cell membrane of a variety of cells, but also on their cytoplasm in a rather high proportion, although in this case its function is not clear.

In this work we have studied if expression of hERG plays a role on DNA damage response using two human cell lines, the HEK293 that does not endogenously express this protein, and the HEK-H36, obtained by permanent transfection of the HEK293 with a plasmid containing the hERG gene, that overexpresses the channel. Both cell types were treated with the monofunctional alkylating agent methyl methanesulfonate (MMS), a genotoxic agent with a well known mechanism of action, and the induced DNA damage was subsequently quantified and compared with the comet assay.

Viability analysis showed that both cell lines were similarly sensitive to MMS. When cells were treated for 3 h with 50, 100, 200 and 350 μM MMS (all concentrations clearly under the respective IC50) to study the DNA damage response, our preliminary results showed that although there were not differences in endogenous DNA damage levels between both cell types, their response to MMS treatment was different, because more DNA strand breaks were induced in HEK293 cells than in the HEK-H36 ones that express the hERG channel. Since this channel is preferentially expressed in some tumour tissues, these results suggest that the expression of this protein may help the cells to respond to the presence of DNA damage, and that it could be used, for instance, as a tool to regulate response to chemotherapy.