

and telomere shortening. Escape from apoptosis also makes cancer cells resistant to chemotherapy and radiation. The molecular machinery of apoptosis is a potential target for drugs that could promote cell death in colorectal cancer cells. The intrinsic (mitochondrial) pathway of apoptosis is regulated mainly the the Bcl-2 protein family, which are activated by various stimuli, including growth factor withdrawal and cellular damage. Under such circumstances, the antiapoptotic factors (eg. Bcl-2, Bcl-XL, Bcl-W, Mcl-1) release the proapoptotic factors (eg. BAK, BAX), which in turn increase mitochondrial membrane permeability, leading to cytochrome C release and Caspase 9 activation and consequently, via Caspase 3 activation, to apoptosis. In cancer antiapoptotic Bcl-2 family members are overexpressed, while the proapoptotic factors are underexpressed. "BH-3 mimetics" are a class of small molecules inhibitors of certain antiapoptotic Bcl-2 family members. Navitoclax is a potent inhibitor of Bcl-2, Bcl-W and Bcl-XL, with in vitro evidence of apoptosis induction in colorectal cancer cells, and demonstrated safety in a phase I clinical trial in combination with established therapy regimes. Obatoclax is a promising pan-Bcl-2 inhibitor. HA14-1 is a small molecule selectively targeting Bcl-2. Oblimersen is an antisense oligonucleotide targeting Bcl-2, and has shown safety in phase I trials. In summary, several new drugs focusing on apoptosis induction in colorectal cancer are currently being studied, which will hopefully lead to better therapies in the future.

Keywords: apoptosis; colorectal cancer; therapy; new drugs.

KIDNEY TUMOR EMPERIPOLESIS

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Emperipolesis means active penetration of one cell by another which remains intact. Main cells participating in emperipolesis usually are histiocytes, but other cell types may participate. Emperipolesis can also be found in some cancers.

The exact mechanism for emperipolesis is not fully known but it is believed that the pathway of lizosom degradation mediated NK ("natural killer") cells is crucial in this process. It was noted that NK cells use emperipolesis when leading tumor cells to programmed cell death. Process similar to emperipolesis, called entosis was also described, but with the different ultrastructural pathways and molecules in-

volved. Fate of the cells after process is done is one of the raised questions. Usually degradation of one cell is seen.

In some epithelial tumors of the kidney emperipolesis was observed. In the last 5 years an entity called biphasic squamoid-alveolar carcinoma of the kidney was described and it has characteristics of papillary renal cell carcinoma with emperipolesis in the near proximity of large cells. The significance of this process in the kidney tumors has not yet been fully clarified.

Keywords: emperipolesis; kidney tumor; biphasic squamoid-alveolar carcinoma.

COMPARISON BETWEEN SURVIVIN AND KI-67 PROLIFERATIVE INDEX IN HER-2 POSITIVE AND TRIPLE NEGATIVE BREAST CARCINOMA

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Survivin is a member of the inhibitor of apoptosis (IAP) family. It is also involved in the regulation of cell division. Survivin is widely expressed in foetal tissues and in human cancers, but generally not in normal adult tissue. Apoptosis is the process of programmed cell death where senescent or damaged cells that are beyond repair are eliminated. It is a cascade of molecular events regulated by proteins that promote or prevent cell death. It is believed to be an important mechanism by which therapeutic chemotherapy and radiation therapy destroy cancer cells. Survivin is an anti-apoptotic protein that is overexpressed in most human cancers. Survivin regulates the G2/M phase of the cell cycle by associating with mitotic spindle microtubules, and it directly inhibits caspase-3 and caspase-7 activity. During tumorigenesis, survivin expression is inversely correlated with apoptosis inhibition and positively correlated with proliferation and angiogenesis. In our previous research, we observed immunohistochemical results of survivin and the relation between survivin and proliferative index Ki-67 in 50 cases of breast cancer in accordance with immunophenotype by St.Galen (2015g.). Survivin immunoreactivity was evaluated semiquantitatively according to the previous studies. Nuclear and cytoplasmic tumour cell immunoreactivities were separately assessed at 40 magnification, and were given an arbitrary score as follows: 0(0-5% positive cells); 1(5-20%); 2(21-50%);