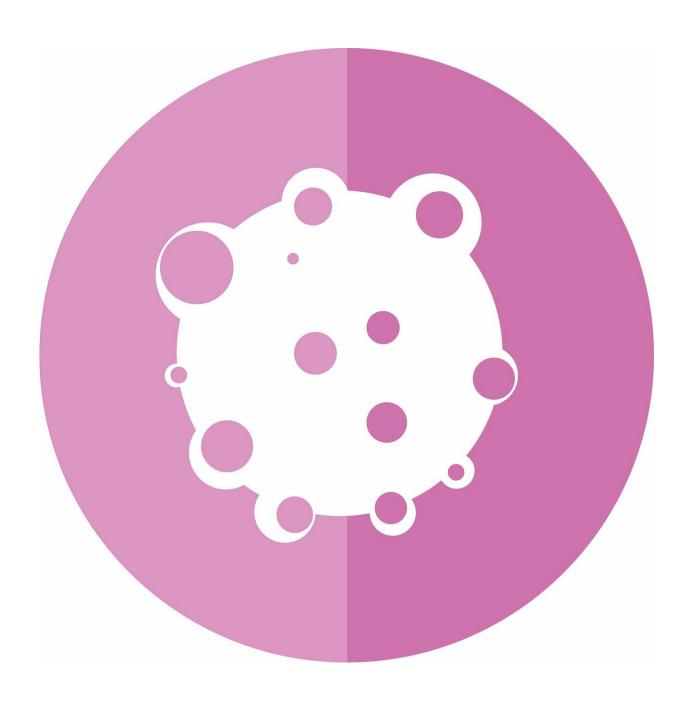


Identification of all types of germ cells tumors

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Germ cell tumors constitute a diverse group of rare tumors, which occur in the testes, ovaries and also in other places. Some germ cell tumors exist prenatally, while others present during or after puberty. The majority are benign. Malignant germ cell tumors most frequently appear in the testicle of adolescent and young adult men. Fortunately, these are treatable; even when metastasized, survival rates are over 80 per cent.

Various germ cell tumors

As the name suggests, germ cell tumors develop from germ cells: sperm cells, oocytes and their progenitors. When an oocyte is fertilized, the development of an embryo is initiated. The fertilized oocyte has the potential to become any other type of cell. Early in development cells lose this ability, and the number of cell types they may become is restricted. "However, in a new individual there needs to be new germ cells that have the potential to become all cell types," explains Dr. Leendert Looijenga (Princess Máxima Center and Erasmus MC). "These cells carry the potential danger of becoming germ cell tumors by spontaneously starting embryonal development."

Different molecular mechanisms need to prevent spontaneous embryonal development by <u>germ cells</u>, since these would result in tumors. Sometimes things go awry in one of these protective mechanisms. "Dependent on which mechanism is affected, we distinguished recently five types of germ cell tumors," says Looijenga. By prolonged studies Looijenga and his colleague Dr. Wolter Oosterhuis (Erasmus MC) gained new insights and expanded the amount of <u>tumor</u> types to seven. They described their finding in the scientific magazine *Nature Reviews Cancer*.



Expansion of the tumor types

One of the newly described categories is type 0. "This is in fact an underdeveloped Siamese twin," says Oosterhuis. "At the points of attachment of the Siamese twins, a second embryo manifests as germ cell tumor. The baby is born with the tumor."

Type 0 and the other five, earlier described types differ from other types of cancer in that they do not arise as a result of mutations in the DNA, but are caused instead by failure of the mechanism that should prevent spontaneous embryonal development.

Germ cell tumor type VI is the only type that is caused by mutations in the DNA. Very infrequently that occurs spontaneously in the body, but more often adult cells are genetically modified in the laboratory for therapeutic purposes, for instance, regenerative medicines. "These cells may only be safely used when we can prevent the development of germ cell tumor type VI," states Looi jenga.

The new insight into the development of germ cell tumors and the division based upon that constituted a solid ground for future epidemiologic, fundamental and clinical research. Moreover, the division is highly valuable in direct patient care. "Treatment sensitivity and also resistance can be mapped more reliably. This may contribute to improved treatments in the future," says Looijenga.

More information: J. Wolter Oosterhuis et al, Human germ cell tumours from a developmental perspective, *Nature Reviews Cancer* (2019). DOI: 10.1038/s41568-019-0178-9

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