Editorial referring to the paper published in this issue on pp. 273–280

UROLOGICAL ONCOLOGY

Stem cells – the key to cancer treatment

Kajetan Juszczak[1,2], Piotr Maciukiewicz[1]

[1]Department of Urology, Rydygier Memorial Hospital, Cracow, Poland

[2]Department of Pathophysiology, Jagiellonian University, Medical College, Cracow, Poland

It is worth mentioning that anti-cancer treatment has entered into an interesting era, with traditional therapies such as surgery, radiotherapy, chemotherapy, and hormonotherapy on one side, and alternative therapies targeting stem cells on the other. Is it a new period for stem cells in clinical practice? Will stem cells become the cornerstone target of urological cancer treatment strategy in the future? Many convincing data indicate: yes. However, further studies are highly required to find the straight answer.

What do we know about stem cells? Well, stem cells are biological cells found in all multicellular organisms that can divide and differentiate into diverse specialized cell types and can self–renew to produce more stem cells. In adult organisms, stem cells and progenitor cells collectively act as a repair system for the body, replenishing adult tissues.

The interest in stem cells in non–cancer and cancer disease is constantly growing. On one hand, hair follicle and bone marrow mesenchymal stem cells (which show high plasticity potential and are able to differentiate into urothelium and muscle layer *in vitro* under defined culture conditions), can be used in urinary tract regeneration [1]. On the other hand, the stem cells seem to participate in carcinogenesis, concerning possibly the primary tumor, local recurrence, or distant metastasis, even if these cells represent only a small proportion of the tumor cell population. Stem cells are under strict control from both intrinsic and extrinsic factors, and loss of this control has been postulated to be a key step in the carcinogenic process. Additionally, Bajek et al. [2] revealed that prostate epithelial stem cells are resistant to apoptosis after α1–antagonist treatment in patients with benign prostate hyperplasia. To maintain homeostasis it is important to keep tight control over stem cell fate [3]. Based on current data, the cancer may be considered as a cancer stem cell disorder rather than that of rapidly growing cells. Although the origin of the cancer stem cells is yet to be defined, the concept of the cancer stem cells may allow new treatment options in the possible cure of the cancer [4, 5]. The authors of this article reviewed the current state of knowledge regarding the achievements in cancer stem cells research in uro–oncology (prostate, bladder, kidney, and testicular cancer), thus presenting convincing evidence that urological cancers are clones of the cells that originate from cancer stem cells. In the pathogenesis of the tumor development, in which the cancer stem cells play a role, three pathophysiological scenarios can be distinguished, as follows: 1) the mutation of normal stem cells or progenitor cells into cancer stem cells can lead to the development of the primary tumor; 2) during chemotherapy most of the primary tumor cells may be destroyed, but if cancer stem cells are not eradicated they become refractory cancer stem cells and may lead to recurrence of tumor; 3) the cancer stem cells may emigrate to distal sites from the primary tumor and cause metastasis [6]. Malanchi et al. [7] showed that a small population of cancer stem cells is critical for metastatic colonization (that is, the initial expansion of cancer cells at the secondary site), and that stromal niche signals are crucial to this expansion process. Furthermore, Ansorgova et al. [8] support the view that a tumor may be considered an abnormal 'organ' where the growth of tumor cells is controlled by a rare sub–population of tumor stem cells, giving rise to both a greater number of tumor cells and non–tumorigenic tumor cells. Moreover, the attention should be given to both tumor stem cells and micro–environment (cancer stem cells' 'niches') for more effective anti-tumor treatment. Also, please note that the fundamental problems encountered in stem cell research are that there is still a distinct lack of detail in defined markers of these cells, until now only a small percentage of the population have studied tumor cells, and the interdependence between the cells and their micro–environment is not conclusively understood. Hypothetically, the identification of the cancer stem cells

may allow the development of treatment modalities that target cancer stem cells rather than rapidly dividing cells in the cancer. This may cure the cancer, as the remaining cells in the cancer growth have limited proliferative capability.

In conclusion. Better understanding of the biology and pathophysiology of a cancer stem cell and its niche's profile within different cancer disease, seems to be crucial for opening up new possibilities for cancer clinical course and treatment.

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Correspondence
Dr. Kajetan Juszczak, FEBU, M.D., Ph.D.
kajus13@poczta.onet.pl