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What is the Possible Role of Stem Cells in the Proposed "Erythrocyte Associated Necrosis Factor" Exploitable in Translational Medicine

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Abstract

The burden of cancer treatment is being lightened by research on target therapy. In this paper, the focus is on the possible utilization of the natural phenomenon of necrosis itself as it was recently discovered in the microenvironment of the thoracic duct. In sum, it is hypothesized that, considering it, a named "Erythrocyte Associated Necrosis Factor" (EANF) plays a significant role. Therefore, with reference to the cancer stem cell system, does it play any part?

Keywords: Cancer; Stem cells; Thoracic duct; Necrosis factor; Target therapy; Cancer cure

Commentary

Cancer has been such a burden on mankind that the quest for its cure has been warming up steadily. In principle, to achieve the necrosis of the cancer cells is sought. In my previous report, [1] I proposed that, what I named as the "Erythrocyte Associated Necrosis Factor" (EANF), can explain the direction which research should take with regard to the target therapy of cancer. In my own words, "it is hypothesized that, if intravital video microscopy is used to obtain subsets of both necrotic and lively cancer cells from the thoracic duct of consenting lung cancer patients, the underlying EANF will definitely materialize." Then I added as follows: "It is predicted that the manipulative replication of this factor in the drug centers will ensure progress." Therefore, I now suggest that the up and coming translational centers must be the better options [2].

Therefore, the question arises as to the possible role of stem cells in this important problem. Consider the possible role of stem cells [3]. According to Mehlen and Puisieux, [4] "one proposed mechanism to explain this inefficiency is provided by the cancer stem cell model, which hypothesizes that micrometastases can only be established by tumour stem cells, which are few in number." Moreover, in the words of Sleeman and Steeg, [5] "there is evidence for a hierarchical organization within tumour cells, the only cells in the population able to initiate the formation of a new tumour." "These cancer stem cells," they continued, "would be expected to contribute decisively to metastasis formation."

Formation and the attendant features of cancer spread were interlinked in the massive review of Coghlin and Murray [6]. Note their last sentence:

Finally, a clearer understanding of the biology of stem-like cells in tumourigenesis and metastasis may reveal vital information about the underlying nature of cancer and, consequently, provide new directions for the development of therapeutic intervention in metastatic disease.

Disease of the cancer genre has invoked the moves to discover target therapy. Now, the stem cell angle has been considered above. Therefore, what of general principles? In fact, Kaplan et al. [7] felt that focusing on the early cellular and molecular events in both dissemination and selectivity ought to lead to new approaches for detecting and preventing metastasis at its earliest inception.

Inception is followed by the formation of new lymphatic vessels, i.e., lymphangiogenesis. For Nagahashis' group, [8] there is need to consider "its clinical application as a biomarker and target for new therapy." Okumura's et al. [9] considered the existence of a "therapy modulation factor," while Poste and Fidler [10] brought in the probability of the existence of the selective growth of specialised subpopulation of highly metastatic cells endowed with specific properties that befit them to complete each step of the metastatic process." On their part, Mazzocca and Cariona [11] were of the view that "the future pharmacological challenge will be to combine drugs that target different aspects of the complex multistep process." In fact, according to Karpanen and Alitaso, [12] "several key questions remain to be resolved, including the relative contributions of different pathways targeting lymphatic vasculature, the molecular and cellular processes of lymphatic maturation, and the detailed mechanisms of tumor metastasis via the lymphatic system."

System of the lymphatics is principally centered on the thoracic duct. As far back as 1798, Cooper [13] was struck by its position in the human economy. However, part of its challenge to researchers has been its sheer length of some 45 cm. However, I circumvented this problem by introducing the mono-block formalin-fixation method of preserving in one piece the entire axial autopsy materials from the neck to the pelvis [14]. Furthermore, through serendipity, I introduced the Swiss-roll technique of coiling the entire duct and processing it on but a single microscope slide [15]. This helped to display metastasizing cancer cells on their way from the cisterna chyli, then through the chest, and back to the circulation.

Circulation is important with respect to the microenvironment of the thoracic duct. Thus, it was found to display not only the subset of lively cancer cells but also the subset of necrotic cancer cells. Note the specificity of my personal citation as follows: "Necrosis of the cancer cells was apparent in three cases, but it was clear that this had occurred in association with large aggregates of the malignant cells and that among such aggregated cells red blood corpuscles abounded." Consequently, an important question arises. What is the possible role of stem cells in the above commingling of cancer cells and red cells? In particular, what significant part does the thoracic duct play? I am persuaded that the answer will emerge if consenting patients are cannulated with the new video microscope [16]. This will ensure the recondite retrieval of the above two necessary research subsets. Thereafter, one possible result

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may emerge in translational laboratories [17] as regards the identifiable factor responsible for this hitherto naturally occurring phenomenon of necrosis. In all probability, if all hands are on the deck as regards stem cell research, [18,19] including all important facilities as well as fundings, [20-22] the target breakthrough should appear sooner than later, and thereby conduce to cancer cure.

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