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On Mechanisms of Carcinogenesis Induced by a Foreign Body (FB-Carcinogenesis)

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Hypothesis

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Introduction

One of the issues that is important for understanding the mechanisms of FB-carcinogenesis is the question of normal sarcoma progenitor cells that occur in the immediate vicinity of implants under the skin of experimental animals (rats, mice). The work described here was done on mice that were implanted with plastic plates .The yield of tumors was about 50% for plates made of polyvinyl chloride with a size of 22x15mm. The average latent period of tumor occurrence is 15 months. This type of carcinogenesis was of great interest to researchers, and many tried to find an explanation for it. I agree with the opinion that the main role in this type of carcinogenesis is played by macrophages that populate the surface of the plate [1]. In 2019, an article was published that showed that the level of expression of proinflammatory cytokines by cells living on the surface of carcinogenic Millipore filters (macrophages) is significantly higher than by macrophages from non-carcinogenic filters [2]. It is possible that the level of expression of Pro-inflammatory cytokines is crucial for the occurrence of tumors, at least in this type of carcinogenesis.

It is shown that a monolayer of macrophages is formed on the plate. Among them are single sarcoma progenitor cells that multiply rapidly when removed from the surface of the plate and transferred to culture in vitro. When subcutaneous introduction of cells of this culture, tumors are formed if the plate was under the mouse skin for a quite long time after implantation. As for tumor progenitor cells: after studying the ultrastructure of such cells, Johnson et al., we came to the conclusion that they are not fibroblasts (as was usually believed earlier), but rather pericytes and have polypotency, since sarcomas are formed of different histological types [3,4]. In 2013, an article was published describing experiments on the cultivation of sarcoma progenitor cells on Matrigel. The cells formed capillary-like structures on the surface of the Matrigel; in a monolayer on a solid substrate, they show "cobblestone pavement" growth [5]. This allowed us to conclude that the origin of sarcomas from endothelial cells is possible. Then we continued the study of cells-F FB-sarcoma by PCR and showed [6], Veg VEGF-a, Veg vegfr2 (flk1) is a marker of the endothelium. Immunochemical Method using monoclonal antibodies obtained a positive result with antibodies to AFM and a negative result for the Willebrand factor. So it's not endothelium, and Johnson and co-authors were right - it's pericytes?.

In 2018, an investigation [7] showed the ability of "vascular endothelial growth factor-a (sefr-a), a specific endothelial cell mitogen produced by various cell types (including macrophages) to induce differentiation of mesenchymal stem cells (MSCS) into endothelial cells.

All of the above Makes it Possible to Make an Assumption

The cells that form sarcomas induced by a foreign body are MSCS (mesenchymal stem cells), which, when they reach the surface of the plate implanted under the skin, differentiate and eventually malignize under the action of surrounding macrophages.

The expression of TFR-beta by macrophages leads to the expression of ASMA by mesenchymal stem cells [8]; the production of VEGF-a by macrophages explains the formation of capillaries on the Matrigel by FB-sarcoma precursors.

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