Kevin Johnson Dr. Steel Cell Biology Bio 293 April 23, 2023

Squamous Cell Carcinoma- Background Essay

Squamous Cell Carcinoma is a cancer that begins in squamous cells. Squamous cells are flat cells that line many areas in the body. The carcinoma cells initially start in a cluster or localized area within specific tissue in the body. The cancer cells form on the surface of the skin and also on the lining of organs in the body or the lining of the respiratory and digestive tracts. This type of cancer accounts for most of the cancer types found in each of the examples below.

Some examples are

Esophageal squamous cell carcinoma which is esophageal cancer

Cutaneous squamous cell carcinoma which is a skin cancer

Squamous cell carcinoma of the lung which is a lung cancer

Squamous cell carcinoma of the thyroid which is a thyroid cancer

Squamous cell carcinoma of the vagina which is a vaginal cancer.

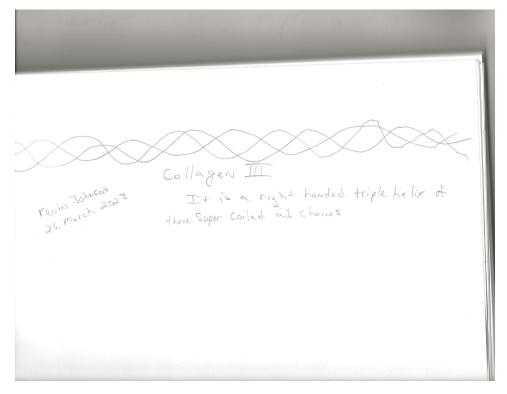
Even though it can start in these areas and in this tissue once it becomes invasive it can metastasis and starts to spread. There are several different subtypes found in the squamous cell carcinoma family of cancer. (Wikipedia contributors, 2023a)

Collagen III or Type III collagen is a protein composed of 3 identical peptide chains each is called an alpha 1 chain of collagen III; The protein is found in your hollow organs like the human liver. It is important to help organs and cells function properly. (Sugita, et al., 2021) It is synthesized by cells as a pre-procollagen. A signal peptide is cleaved off to produce a procollagen molecule. Three of the type III procollagen chains come together at carboxyl terminal ends; the structure is stabilized by forming disulphide bonds. Then each chain folds into a left-handed helix. During this process each goes through several post translational modifications as the monomers are being translated. Each chain then wraps together into a right-handed super helix called a triple helix. (Wikipedia contributors 2023b)

In one study they found that collagen III might help with suppressing the carcinoma tumor by walling off the tumor cells or be produced by the tumor cells the researchers were unsure they found depending on the type of carcinoma they might have lesser results or no results when introducing collagen. (Kumari, et al., 2017) While some research makes it seem as if collagen III

may be able to assist patients that have squamous cell carcinoma; the research is not conclusive. There is also research that shows that collagen rich environments can encourage Hypoxia which can intensify cancer progression. Unfortunately, we still have a lot of research to do to determine if collagen III is more benefit or not in treating and controlling cancer. (Xu, et al., 2019)

Collagen III is a homotrimer that contains three a1 chains all supercoiled around one another in a right-handed triple helix. (Nielsen, Karsdal, 2016)



In the image above you see the right-handed triple helix that is formed out of the three a1 chains.

In looking at the paper 'A tumor-derived type III collagen-rich ECM niche regulates tumor cell dormancy' (Di Martino et al., 2021) and the data collected; They looked at the Extracellular Matrix (ECM). They found that in the dormant cells they were surrounded with a mesh like cluster of collagen III cells. Whereas in the proliferative tumors there was less collagen III present, and the cells were growing more rapidly. In removing the tumors and checking the sites again later they found that the tumor cells were growing back and there were more linear cells and less mesh like cells present of collagen III. (Di Martino et al., 2021)

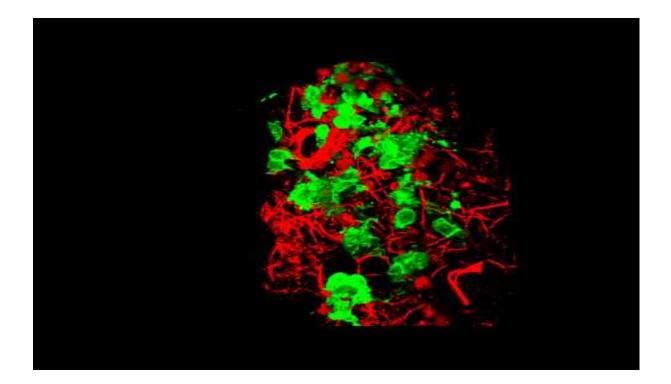
The single cell compared to the metastases cancer cells also showed a difference. The single cell showed more of a shell or mesh of collagen III than the metastases which showed more of a

linear cell structure. When looking at the images you could tell the difference in growth due to the color differences there was a lot more yellow(overlap) in the single cell than there was in the metastases meaning that the metastases was growing at a faster rate. The single cells really did not appear to be going through a large growth or rapid growth cycle. It is still showing in a G1 phase in both the tumor and residual tumor cells of the single cells. The metastatic cells though show the cycle is continuing and is at that point looks like it is in a S phase The images showed more of the growth cycle in the metastatic tumors than the single cells. The cycle was faster when looking at the 2 images, the first with just the cell and the second with the collagen III overlaid. (Di Martino et al., 2021) Around the single cells you see a lot more collagen III in that mesh configuration whereas in the metastases the collagen III cells were more linear and less present.

In another test the data showed that collagen III could help to reduce or inhibit the growth of the proliferative T-HEp3 cell line. They used a control that was saline and then a test with collagen III and one with collagen IV. In the test the control tumor seemed to grow normally after being injected with saline. They noticed a remarkably different result in the tumor injected with collagen III. The tumor grew a lot slower and seemed to have reduced or inhibited growth. The collagen IV was close in results to the saline or control tumor. This supports the theory that collagen III can inhibit the growth or slow down the growth cycle of prolific cancer like T-HEp3.

It does appear that collagen III helped slow down and decrease the number of cells going through the growth cycle in S/G2. Based off the research in this paper it can be concluded that collagen III can have a positive effect on reducing the size and growth of tumors of a specific type of cancer. There will still need to be further tests to determine if there are ways to increase the response that tumors have on specific types of cancer cells and tumors.

Cancer cells on lung collagen in 3-D



https://youtu.be/FO3Uqe0UGnM

Clip by marcuslab found on YouTube this is a 3-D image of cancer cells found in the lungs of mice.

Citation page

- 1. Wikipedia contributors. (2023a). squamous cell carcinoma https://en.wikipedia.org/wiki/Squamous-cell_carcinoma
- Sugita, S., Suzumura, T., Nakamura, A., Tsukiji, S., Ujihara, Y., Nakamura, M. (2021) "Second harmonic generation light quantifies the ratio of type III to total (I III) collagen in a bundle of collagen fiber," *Scientific reports*, 11(1), p. 11874.
- 3. Wikipedia contributors. (2023b). Collagen, type III alpha 1 https://en.wikipedia.org/wiki/Collagen, type III, alpha 1
- Kumari, K., Ghosh, S., Patil, S., Augustine, D., Venkatesiah, S.S., Rao, R.S. (2017) "Expression of type III collagen correlates with poor prognosis in oral squamous cell carcinoma," *Journal of investigative and clinical dentistry*, 8(4), pp. e12253-n/a.
- Xu, S. Xu, H., Wang, W., Li, S., Li, H., Li, T., Zhang, W., Yu, X., Liu, L. (2019) "The role of collagen in cancer: From bench to bedside," Journal of Translational Medicine, 17(1). Available at: <u>https://doi.org/10.1186/s12967-019-2058-1</u>.
- Nielsen, M.J. and Karsdal, M.A. (2016) "Chapter 3 Type III Collagen," in Biochemistry of Collagens, Laminins and Elastin "Structure, Function and Biomarkers". Academic Press, pp. 21–30.
- Di Martino, J.S. *et al.* (2021) "A tumor-derived type III collagen-rich ECM niche regulates tumor cell dormancy," *Nature Cancer*, 3(1), pp. 90–107. Available at: <u>https://doi.org/10.1038/s43018-021-00291-9</u>.