Targeting dynamic migratory response to electric fields to specifically segregate cancer cells

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Abstract

Cell migration, a fundamentally required biological function, can be controlled by chemical gradients (chemotaxis), the presence of adherent ligands (haptotaxis), mechanical stiffness (durotaxis), and applied electrical fields (electrotaxis) as well as other factors. While each type of directed movement serves specific physiological roles, the cellular response to electrical fields has been shown to be an overriding stimulus, at least in the case of wound healing [1]. The proposed explanation of this behavior concerns the presence of an electrical charge gradient between the basal and apical layers of healthy epithelium which, when broken, short circuits and provides an external stimulus which can be sensed by nearby cells. Likewise, other physiologic systems generate such voltages, including the tumor environment which may increase the likelihood of cancer metastasis from the primary tumor [2]. These endogenous electric fields have potential for use in the detection of tumor growths in living tissue.

We have utilized the platform developed by the Zhao group to apply electric fields of varying strength to confirm the electrotactic behavior of the highly metastatic cell line MDA-MB-231 and have begun analyzing the behavior of its non-transformed counterpart MCF-10A [3]. Surprisingly, both cell lines undergo electrotaxis towards the anode within the electrotactic chamber, whereas the transformed but non-metastatic cell line, MCF-7, is reported to experience weak electrotaxis towards the cathode [4]. These results suggest that the role of electrotaxis changes throughout cancer progression, possibly becoming involved in migration during metastasis.

Chemotherapy, a conventional cancer treatment, has only been shown to be responsible for contributing to the 5-year survival rate of only 2.1% of malignant cancers in American adults, showing a clear need for alternative methods of treatment [5]. It also effectively selects chemotherapeutically resistant cells in a Darwinian fashion, making recurring cancers more dangerous. Utilizing the electrotaxis associated with cancer, this work aims to provide a method by which cancer cells would be isolated from healthy tissue in such a way that more highly metastatic and resistant cells would be less likely to survive *in vivo*. To test this, we will develop one of the first reported methods of separating cells which maintain their natural state of adhesion to a solid substrate, unlike methods that require cells suspended in a liquid medium such as dielectrophoresis, sedimentation, or centrifugation. Therefore, we envision that this method could be applied *in vivo* to capture metastatic cells.

References

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