

Scientific Paper:

Nature Communications (2018) 9:4545

Redox regulation of EGFR steers migration of hypoxic mammary cells towards oxygen

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Abstract:

Aerotaxis or chemotaxis to oxygen was described in bacteria 130 years ago. In eukaryotes, the main adaptation to hypoxia currently described relies on HIF transcription factors. To investigate whether aerotaxis is conserved in higher eukaryotes, an approach based on the self-generation of hypoxia after cell confinement was developed. We show that epithelial cells from various tissues migrate with an extreme directionality towards oxygen to escape hypoxia, independently of the HIF pathway. We provide evidence that, concomitant to the oxygen gradient, a gradient of reactive oxygen species (ROS) develops under confinement and that antioxidants dampen aerotaxis. Finally, we establish that in mammary cells, EGF receptor, the activity of which is potentiated by ROS and inhibited by hypoxia, represents the molecular target that guides hypoxic cells to oxygen. Our results reveals that aerotaxis is a property of higher eukaryotic cells and proceeds from the conversion of oxygen into ROS.

Keywords: Aerotaxis, HIF pathway, oxygen gradient, hypoxia, eukaryotic cells, EGF receptor