Microfluidic Labyrinth to Explore Non-Adherent Cell Movement

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Leukemia is a predominant cancer type among young individuals, with over 5,000 new pediatric cases annually linked to the BCR-ABL1 fusion gene, signaling a poor prognosis. This fusion gene results from a chromosomal rearrangement that combines two distinct elements: ABL1 and BCR. The ABL1 protein, known for its increased tyrosine kinase activity within the chimeric forms, has been the focus of extended research for many decades. Unlike the well-studied ABL1, the BCR component has received less attention, largely because of its intricate involvement in cellular functions and interactions. This is especially true regarding its interactions with the small GTPases of the Rho family, which are crucial for controlling the organization of the cytoskeleton and, thereby, play a vital role in dictating cell shape and movement. Our research aims to dissect the role of BCR in Rho GTPases-related cellular processes and its potential role in leukemia. We aim to explore how BCR contributes to Rho GTPases homeostasis in blood cells and if alterations in lymphocyte shape and polarity are caused by BCR dysfunction in BCR-ABL1 positive leukemia. To achieve this, we employ cutting-edge imaging techniques, including time-lapse and Total Internal Reflection Fluorescence (TIRF) microscopy, allowing us to characterize non-adherent cell movements and the effects of BCR expression and localization on these processes. Innovatively, we will introduce a microfluidic device designed with optimized labyrinth-like channels that mimic various microenvironments. This setup will enable us to observe blood cell responses to different stimuli, such as chemokine gradients, offering insights into cellular movement patterns under physiological conditions. By delving into the role of the BCR protein in cell motility, especially within the leukemia context, we aim to fill a critical knowledge gap. Our innovative microfluidic device, with its unique labyrinth-like channels, represents a breakthrough in studying cell movement, setting the stage for groundbreaking therapies in pediatric leukemia. With Project FluidMov, we stand on the brink of uncovering new pathways to combat leukemia, potentially revolutionizing treatment for the youngest patients afflicted by this disease.

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