*For Office Use Only*

Tracking No:

Lead:



**PM Initiative Submission Form**

PM initiatives are to be created to represent emerging or established areas of scientific excellence. These initiatives can span across one or more programs, which are listed on the PM Intranet. Each initiative must include a minimum of three scientists, and the lead scientist must hold an appointment at the PM Research Institute. Lead scientists, and team members may belong to multiple, or no initiatives.

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| **Date of Submission:**  | **04 Feb, 2020** |
| **Lead Scientist:** | **Brian Raught** |
| **Other Team Members:** | **Linda Penn, Razq Hakem** |
| **Initiative Title:** | **Creating a BioID mouse** |

**Please include a ‘Vision Statement’ below that describes the focus and scientific goals of the initiative (300 words maximum):**

Proximity-dependent biotinylation (BioID) has revolutionized the study of protein-protein interactions and organellar proteomics. (The Raught lab has published >45 papers to date using this technology, including multiple publications with Drs. Penn, Hakem and many other PM researchers.) BioID is conducted by fusing a mutant *E. coli* biotin ligase (BirA\*) to a “bait” protein of interest. Expression of this fusion polypeptide in a relevant biological setting results in the covalent biotin labeling of proteins in the vicinity of the bait, allowing for the capture and identification of interacting partners in the context of a living cell. As compared to standard affinity-based purification approaches (e.g. IP-MS) BioID can: (i) identify interactions with and amongst membrane proteins, chromatin-associated proteins, and other polypeptide classes that are less amenable to study by standard pulldown techniques; (ii) enrich for transient and/or low affinity interactions (particularly important for e.g. the study of E3 ubiquitin ligase – substrate interactions), and; (iii) provide deep insight into the organization of membrane-less organelles and other subcellular structures that cannot be easily isolated or purified using standard biochemical approaches.

To date, this approach has been limited to use in 2D cultured cells. We (Raught and Penn) conducted the first BioID study in a mouse model, using human xenografts expressing a BirA\*-tagged c-MYC protein. While this approach represented an important first step in characterizing the MYC interactome *in vivo*, the creation of an all-purpose “BioID mouse” will represent a quantum leap in our ability to identify and characterize protein-protein interactions in a living organism, and allow *e.g.* the simultaneous characterization of protein interactomes in multiple tissues and organs in the same animal, the study of protein interactomes throughout multiple stages of animal development, and allow us to monitor protein-protein interactions in animals treated with *e.g.* anticancer drugs or small molecule inhibitors.