

2018 Research Week Proposal

Title – Designing New Cell-membrane Permeable Fluorescent Dyes

Program of Study – Cell and Molecular Biology

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Category – Theoretical Proposal

Abstract: The cell membrane serves as the barrier between the cell and its environment, and is therefore essential to the survival of the cell. However, it represents a significant barrier to staining and tagging the organelles contained therein. It is particularly useful to be able to visualize DNA through fluorescent microscopy. Locating DNA in the cell is useful for observing the mechanisms behind cell division and chromosome replication, and can be used to determine the internal organization of the nucleus. However, these processes cannot be adequately observed if the cell must be broken in order for these components to be accessed and stained.

Since fluorescence microscopy is a key technique in analyzing cells and their components, the ability to tag subcellular structures is the driving force behind the development and testing of new dyes. Many fluorescent dyes exist that can stain DNA in broken (lysed) cells, and these are commonly used in procedures such as gel electrophoresis. The most common example of this type of dye is ethidium bromide, which incorporates itself into the structure of DNA, a process referred to as intercalation. Some dyes can only enter lysed cells, or else their entry must be mediated by transport proteins. The most useful dyes are those that can enter the cell without permanently disrupting the cell membrane.

The proposed research involves the *de novo* design of a cell-permeable fluorescent dye for DNA staining. The first part of the research is the analysis of commonly used fluorescent

cell-staining dyes. Three major components are examined in relation to the structure of the molecules: fluorescence, DNA binding, and cell permeation. As each of these aspects is examined, patterns begin to emerge, indicating common features that should be incorporated into the novel dye. An anthraquinone-based dye is then proposed, and the fluorescence, DNA binding and cell-permeating abilities are predicted. Various techniques will be explored in order to add two different substituents to a single anthraquinone core. The molecules must then be analyzed to determine if the substitution was successful. The excitation and emission wavelengths of the dyes produced will be measured and compared to one another and to commercially available stains. The dyes will be combined with DNA and tested with gel electrophoresis to determine whether or not they bind to DNA as predicted. Finally, the dyes should be tested with live cells to determine whether or not they permeate the cell membrane. This is a key feature that will allow the dyes to be applied in live cell research.