LS17-051 - 3C - Cellular Color Chart

Abstract

In the 3C chemical biological project we screened 90,000 compounds from a diverse chemical compound library for their fluorescence within human cells using an automated highthroughput fluorescent microscopy approach. The aim was to identify fluorescent scaffolds to improve their properties by synthetic chemistry, with the ambition to complement existing dyes. Such new fluorescent dyes might be used for cell biology and perhaps even clinical diagnostics. Currently, the compounds that are available to identify specific subcellular structures or to identify cellular types by fluorescence microscopy are quite limited. Amongst the more than 200 hits that showed intracellular fluorescence we identified several similarities which allowed for a classification of the compounds into different chemical scaffolds.

Through synthetic chemistry we added fluorescence-modifying moieties and thereby generated several analog derivatives for each scaffold. The aim was to modify their emission wavelengths and quantum yields. This novel collection of compounds we investigated for their properties with respect to cellular and subcellular specificity and color. Several novel compounds showed specificity to selected cell lines and cancer cell types. Through hydrothermal synthesis we generated a series of similar compounds (based on the quinoxalines scaffold) that encompass the spectrum from blue to green to yellow. We also synthesized imidazole derivatives amongst which there are several pH sensitives dyes.

Additionally, we developed a method to create a large set of fluorescently labelled proteins within cells to allow for their visualization as well as determination of their abundance and subcellular localization. This serves also validation of the intracellular localization as well as potential cellular target of the novel dyes. This method as well as the properties of the dyes will aid cell biology studies which aim at cell type identification, intracellular localization identification, and intracellular pH measurements.

Scientific disciplines:
Chemical biology (60%) | Organic chemistry (20%) | Cell biology (20%)

Keywords:
fluorescent molecules, intracellular stains, target identification, live cell imaging

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Further links to the persons involved and to the project can be found under
https://www.gmbh.wwtf.at/funding/programmes/ls/LS17-051/