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FULL ARTICLE

A molecular imaging analysis of Cx43 association with Cdo during skeletal myoblast differentiation

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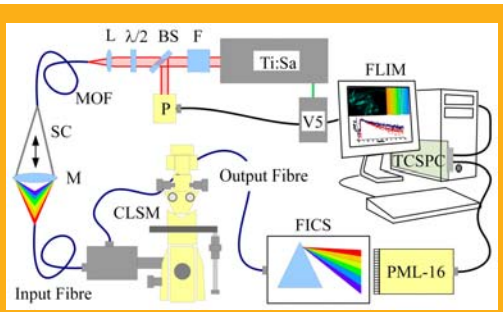
Cell-to-cell contacts are crucial for cell differentiation. The promyogenic cell surface protein, Cdo, functions as a component of multiprotein clusters to mediate cell adhesion signaling. Connexin 43, the main connexin forming gap junctions, also plays a key role in myogenesis. At least part of its effects is independent of the intercellular channel function, but the mechanisms underlying are unknown. Here, using multiple optical approaches, we provided the first evidence that Cx43 physically interacts with Cdo to form dynamic complexes during myoblast differentiation, offering clues for considering this interaction a structural basis of the channel-independent function of Cx43.



Hyperspectral FLIM FRET setup.

1. Introduction

The study of cell signalling pathways is of particular interest for the identification of specific interactions between proteins and other cellular components. Fluorescence microscopy has become a powerful technique to probe such cellular activity, because it allows the selective and specific detection of molecules at low concentration levels [1]. Intensity images, however, only reveal cellular organization, while functional measurements such as fluorescence lifetime imaging (FLIM) can probe cellular activity and protein interactions in a single cell. For a complete study on cellular activity, a combination of fluorescence measurements is needed: intensity, lifetime, and spectral imaging.

In the recent years much attention has been drawn to the role played by several classes of intercellular junctional proteins and related signaling in the cell-contact-based regulation of myoblast differentiation [2].

Skeletal myoblasts are undifferentiated mononuclear precursor cells which are responsible for postnatal muscle growth and injury-induced muscle regen-

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