Characterization of stem cells differentiation using Quantitative Phase Imaging

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We describe the use of quantitative phase imaging (QPI) [1] to classify stem cells according to their differentiation stages without any labelling.

Quantitative phase imaging techniques [1-4] are used in microscopy for imaging semi-transparent samples such as cells and tissues and gives information about the optical path difference (OPD). It generates highly contrasted without any labelling, which enables measuring morphological parameters. OPD also leads to sample dry mass and dry density measurement. The strength of those techniques is their non-invasive and fast approach.

We will show that the high contrast brought by Quadri Wave Lateral Shearing Interferometry and artifacts free imaging allows cellular segmentation from which we can deduce different morphological parameters of interest and make quantitative (i.e. dry mass and mass density) measurements.

The study is realized on iPS cell line PFX#9 stem cell colonies. The whole colony is imaged using a low magnification screening (2.5x and 5x) with laser illumination. Then non-supervised classification methods are used to identify the differentiation stages. We demonstrate that QWLSI allows assessing the homogeneity of the stem cell population and automatically identifying undifferentiated pluripotent stem cells (PSC) in a two-dimension culture from other cells under differentiation. We also show that we can distinguish between 3 types of colonies of iPS cell line PFX#9 in function of their differentiation state and highlight differentiation points using a new image representation.

This information can be useful to detect a partly differentiated colony that shall be removed prior to passage in order to maintain or expand undifferentiated cells. This can also help studying culture medium and experimental conditions effects on stem cell growth and viability.

[1] P. Bon, G. Maucort, B. Wattellier, and S. Monneret, "Quadriwave lateral shearing interferometry for quantitative phase microscopy of living cells", *Opt. Express*, vol. 17, pp. 13080–13094, Jul 2009.