Analysis of stem cells by synchrotron FTIR microspectroscopy

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Stem cells are defined by 3 criterions: they are undifferentiated cells, immortal cells that self-renew indefinitely by symmetric division, and totipotent cells that can differentiate in many varieties of mature cells. Potential applications of stem cells range from regenerative medicine to *in vitro* disease models for pharmacology studies and drug screening, and to creation of tailored models of cell development in cell biology. Stem cells originate from a variety of sources: embryo (ESC), foetus, amniotic liquid, umbilical cord blood, adult tissues (ASC) such as brain, bone marrow …, and from cells forced to de-differentiate by gene transfer (iPSC), nucleus transfer, or chemicals. These different types of stem cells may have different properties, for example ASC are known to differentiate only in a few types of mature cells from the same lineage, and thus full characterization of their properties is required for future applications. Full characterization of a stem cell line is difficult as it should involve genomic analysis (nuclear and mitochondrial), proteomic analysis, SNP profile, HLA profile, kariotyping, gene expression characterization, and the characterization of the differentiation potential i*n vitro* and *in vivo*.

FTIR spectroscopy has been shown to provide a chemical fingerprint of biological cells that can be used for identification and can be correlated to the physiological state of the cells and to their biological properties. Most of the works published so far on stem cells used FTIR spectroscopy to monitor the differentiation of stem cells. In this work we applied a different approach: we tried to characterize different stem cell lines to determine if 1) there exists a specific spectral signature of stemness, 2) different stem cell lines can be differentiated by their spectral signature 3) iPSC regain the spectral signature of their parent ESC 4) the spectral signature is correlated to the differentiation potential.

Stem cells are small, typically 12±2µm in diameter, and synchrotron based FTIR microspectroscopy enables the analysis of individual stem cells included in colonies of hundreds or thousands of cells quickly and with good spectral quality (SNR). Colonies are grown directly on low-e reflective slides and hundreds to thousands of spectra of individual cells can be recorded daily. Multivariate statistical analysis is used to analyse the results. 4 human ESC lines, 4 mouse ESC lines, 6 human iPSC lines and 1 mouse iPSC were analysed.
The results show that each stem cell line presents several spectral signatures depending on the stage in the cell cycle; it is possible to differentiate between cell lines on the basis of their infrared spectrum; stem cells have a different spectral signature from mature cells; iPSC cells effectively regain the spectral signature of their parent stem cells.
One can envision the creation of a database of stem cell spectra which will allow establishing if there exists a correlation between the differentiation potential and the spectral signature.