Quantitative image analysis of cell reprogramming

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Mammalian nucleus is highly compartmentalized for gene functions, and numerous sub-nuclear structures exist. When cells undergo differentiation, senescence and diseases, their nuclear morphologies change specifically. The chromatin and the nucleus have served as good indicators in pathological diagnosis.

Although biological images are difficult to quantify due to their complexity, technologies for computational analyses have advanced. A supervised machine learning algorithm, wndchrm (weighted neighbour distances using a compound hierarchy of algorithms representing morphology), is a multi-purpose pattern recognition tool, which has been developed for classification and mining of image similarities. Wndchrm users define classes by providing example images for each class; type-A or type-B cells, for example. A large set of image features for each image in the defined classes are computed, and image features that are informative for discriminate the classes are selected based on Fisher discriminant scores to construct a classifier, all in an automated fashion. The dataset is tested by cross validations to measure classification accuracy and class similarity which can be visualized with phylogenetic tree.

We have utilized wndchrm to several biological problems, including non-invasive evaluation of cell reprogramming. We could distinguish bona fide iPSCs from improperly reprogrammed non-iPSCs with high accuracy, and localize discriminative image features in cell structure. Extensive analysis of nuclear morphologies revealed sub-nuclear structures typical to iPSCs. Our data revealed that proper cell reprogramming accompany dynamic nuclear and chromatin reconstruction.

References

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