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Automated Image-Based Discrimination of Human Embryonic Stem

Cell Differentiation Status 以雙光子雷射顯微方法區分人類胚胎幹細胞與成體細胞

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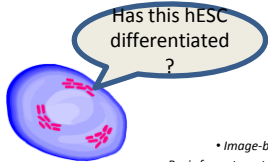
工業技術研究院 Industrial Technology Research Institute, Hsinchu Xian, Taiwan



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Research Question



Q: Can the differentiation status of a human embryonic stem cell (hESC) be determined reliably and automatically?

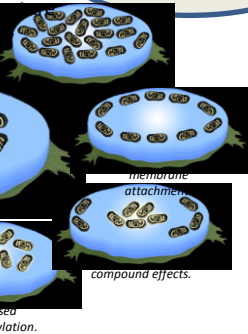
- High-throughput cell culturing for clinical therapies.
- Image-based registration: no need to lyse & stain cells...
- Basis for automated, unsupervised computer dissectors

NON-INVASIVELY

The "smoking gun."

We're going to need some clues...

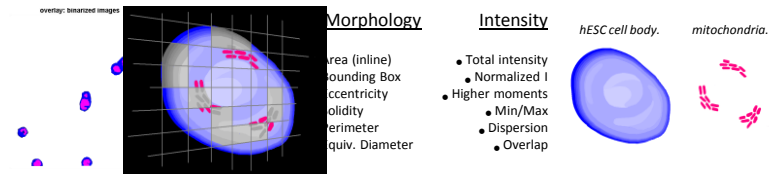
hESC mitochondria exhibit size or activity changes in size or activity (oxidative phosphorylation) during differentiation.



My interest in the NIH lies in the Genes, Cognition, and Psychosis Program (GCAP) of the Clinical Brain Disorders Branch @ the NIMH.

Parallel Feature Extraction

Early-passage HES1-1 (NIH: ES01) cells cultured on mouse feeder cells in various media. 2 microscopies: Bright field (BF) for cell body extraction, 2-Photon (2PM) for mitochondria



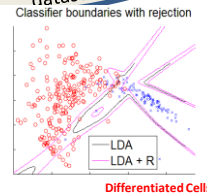
Affine-robust features were extracted from binarized BF (blue) and 2PM (red) images

$$Z_n^m(\rho, \varphi) = R_n^m(\rho) \cos(m\varphi) \quad Z_n^m(\rho, \varphi) = R_n^m(\rho) \sin(m\varphi) \quad R_n^m(\rho) = \sum_{k=0}^{(n-m)/2} \frac{(-1)^k (n-k)!}{k! \binom{(n+m)/2 - k}{(n-m)/2 - k}} \rho^{n-2k} \quad \text{Zernike Polynomials}$$

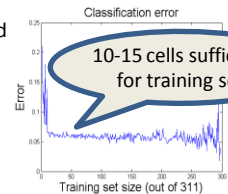
Differentiation (status) determined post-hoc via SSEA-4 on location-keyed images.

94% accuracy on reduced-dimensionality datasets

Preliminary Results



47-D dataset transformed to 2-D set via LDA.



Linear discriminant analysis (LDA) preferred to principal components analysis (PCA): want to perform a supervised analysis via classification error, not maximum variance.