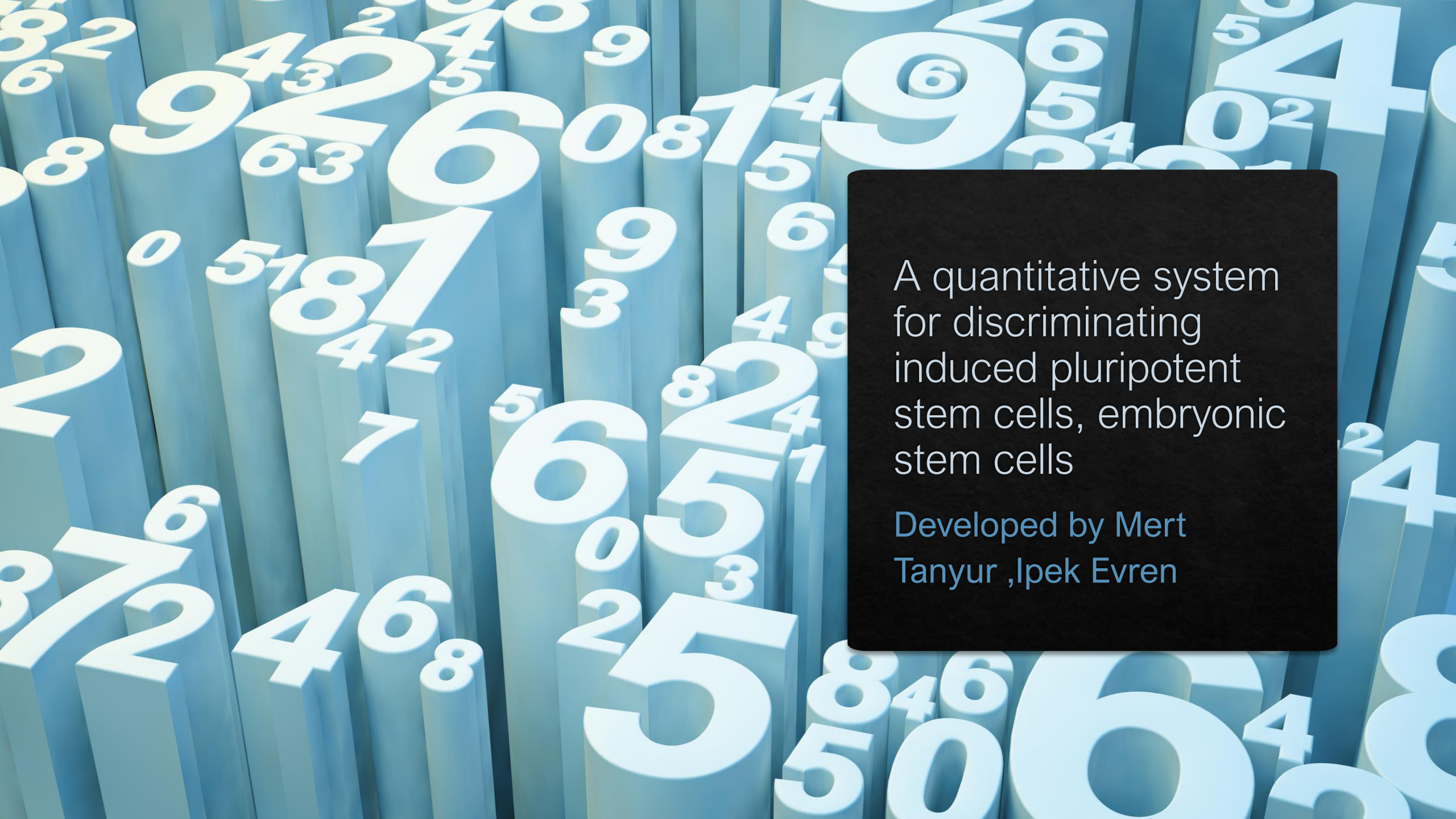
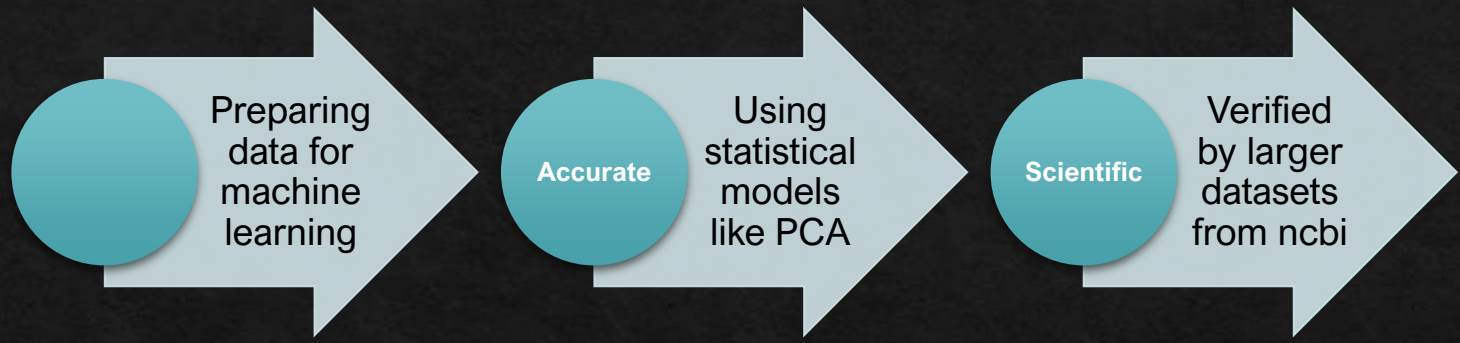


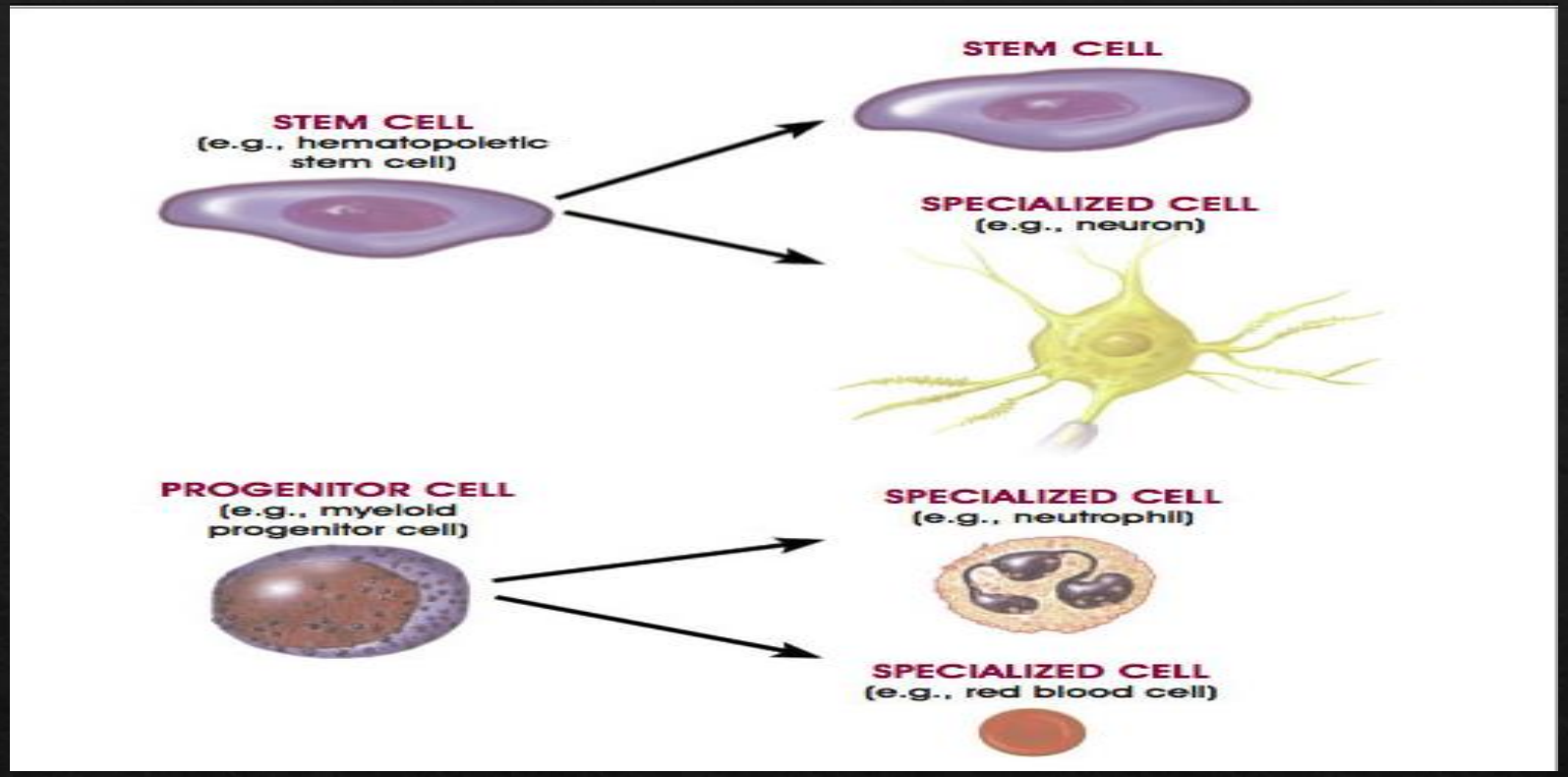
A quantitative system for discriminating induced pluripotent stem cells, embryonic stem cells

Developed by Mert Tanyur ,Ipek Evren

Distinguishing stem cell types by methylation rate



Key words: biomarker, artificial neural network, support vector machines, induced pluripotent stem cells, embryonic stem cells, somatic cells, mathematical models



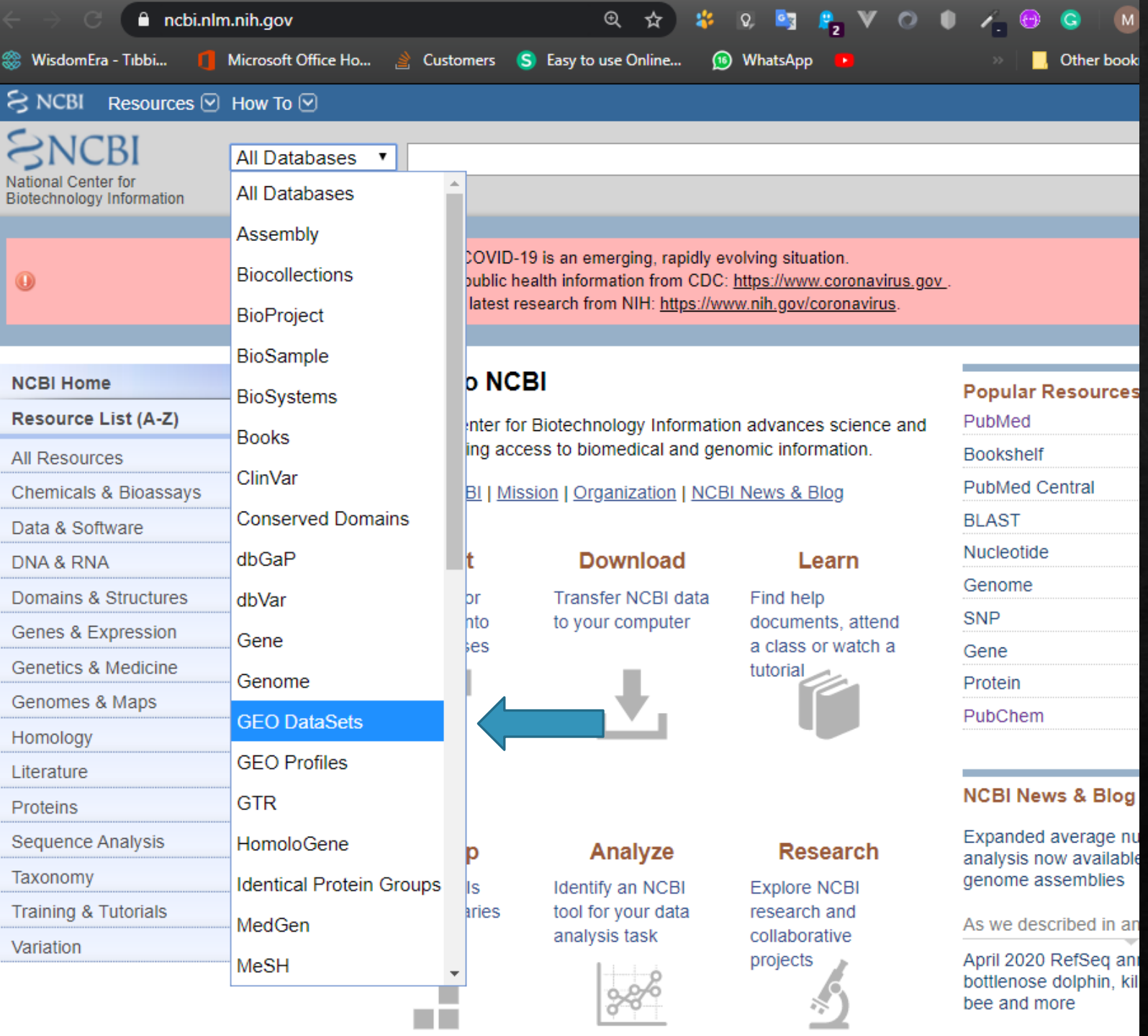
Abstract: Embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs) derived from somatic cells (SCs) provide promising resources for regenerative medicine and medical research, leading to a daily identification of new cell lines. However, an efficient system to discriminate the cell lines is lacking. Here, we developed a quantitative system to discriminate the three cell types, iPSCs, ESCs and SCs. The system contains DNA-methylation biomarkers and mathematical models ,including PCA.

Old but not gold

Traditionally, biomarkers derived from well-characterized individual molecules have been used to distinguish somatic cells (SCs) versus pluripotent cells (PCs), including iPSCs and ESCs [6,7]. PCR and immunostaining can be used to further aid the biomarkers in distinguishing SCs from PCs [6]. However, applying the biomarkers to inherent multipotent cell lines could mislead the results due to the instabilities of multipotent cell lines that vary with conditions [7]. For examples, the OCT4 biomarker, which was once thought to be an excellent marker for discriminating ESCs and SCs, is only transitionally expressed in ESCs and is not consistently expressed in different ESCs, especially in old ESCs [7]. Any single biomarker that was selected from a very limited number of samples is unlikely to be robust enough to classify novel stem cells when applied alone across various conditions [7]. In addition, most of the current biomarkers based on antibodies will fail to detect the protein signals that are of low abundance, and thus the antibody-based biomarkers naturally exhibit low sensitivity. The strategy developed for distinguishing SCs from PCs also may not work for discriminating ESCs and iPSCs due to their similarity.

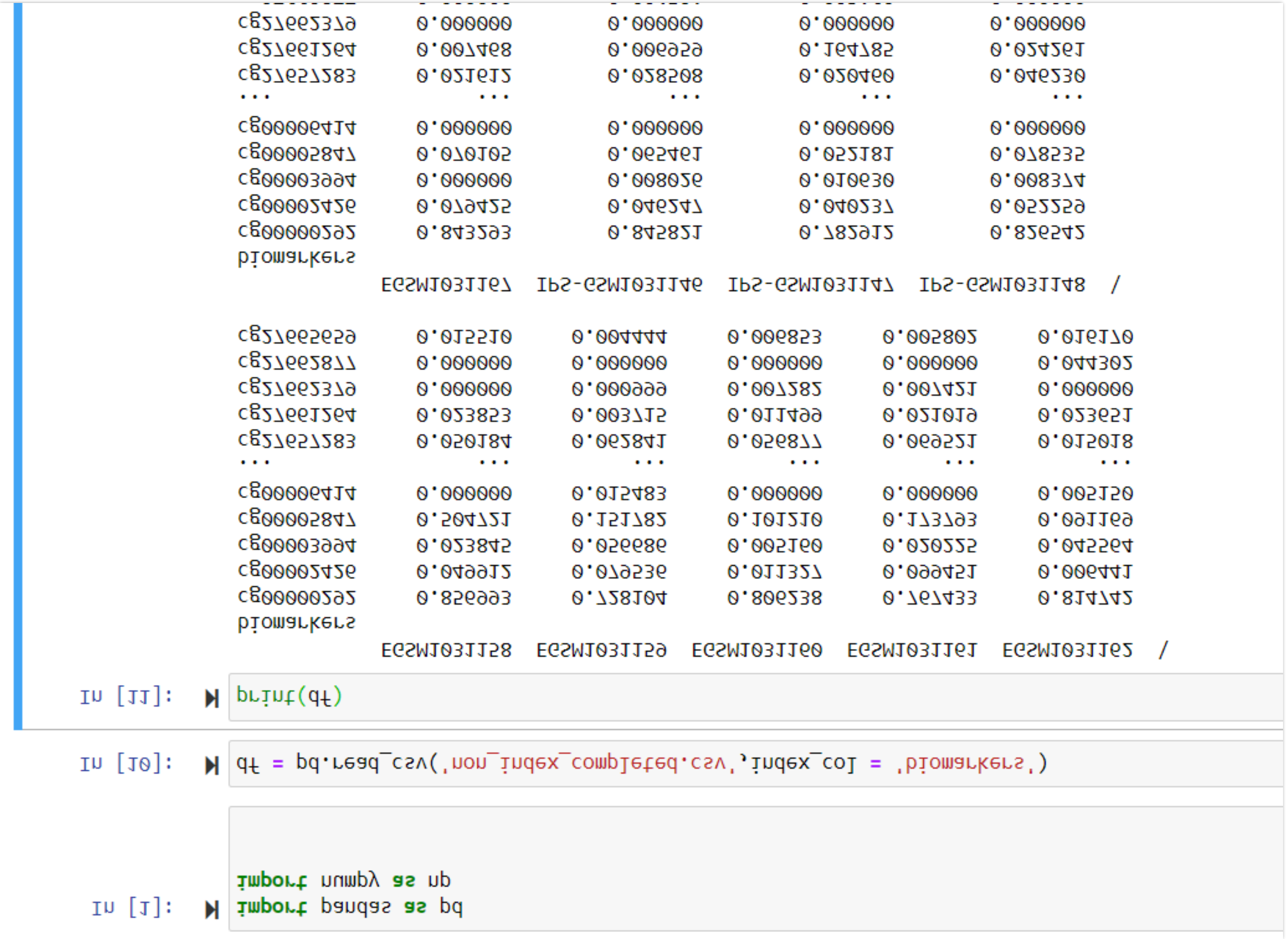
Statictics rocks!

Biomarkers are selected unbiasly with PCA analysis.With 30 biomarkers ,or even with as few as 3 top biomarkers this system can discriminate ESCs from iPSCs with almost %100 percent accuracy.

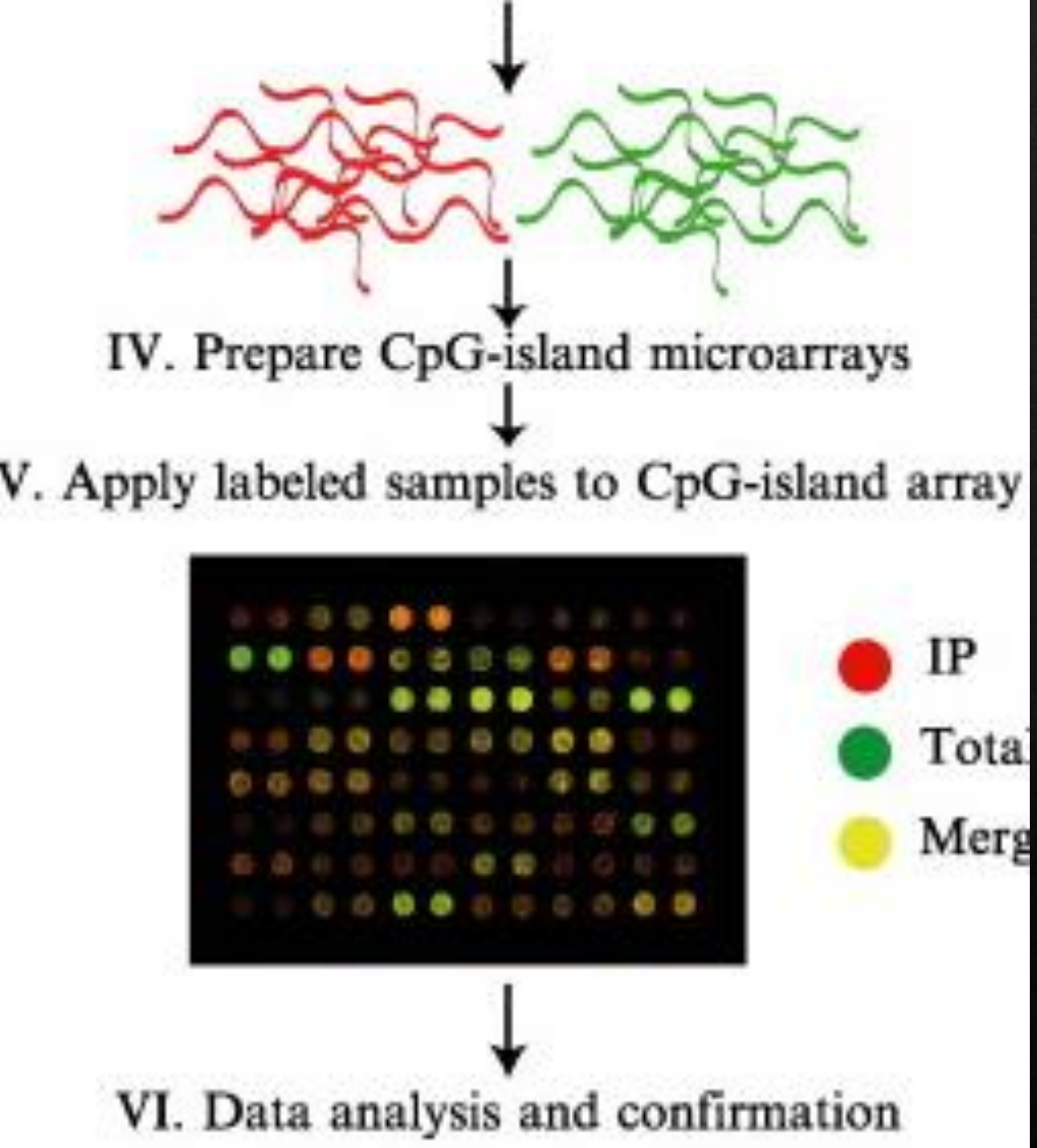


Methylation microarrays were downloaded from GEO databes.

Data pre-processed by python.



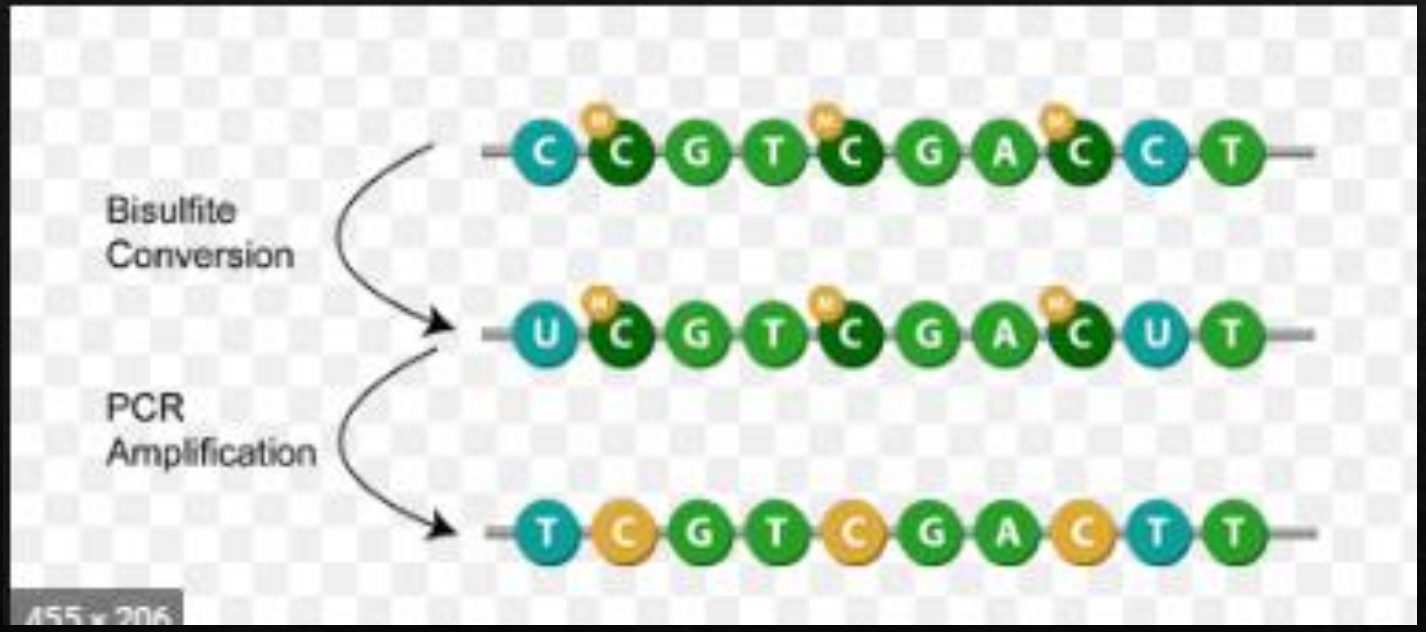
We used human methylation datasets



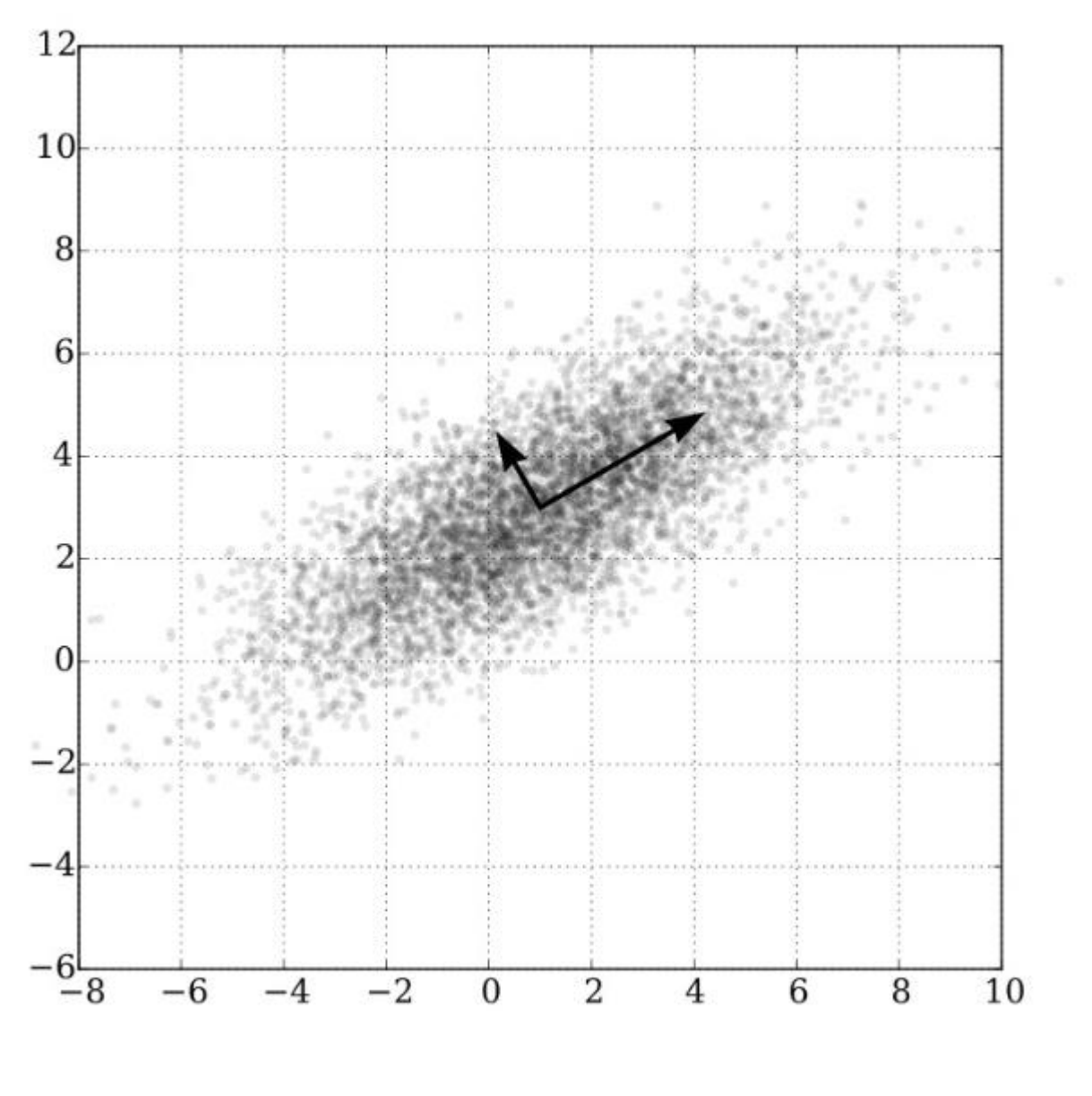
Lab-Method

- Methylation values measured as beta value ranging from 0
- CpG islands indicate the methylation regions.
- Two different colored beam is used to obtain a methylation intensity.

Bisulfite conversion is used to identify methylated bases.



How pca graphics look like



Some Statistical Terms

- Principal components analysis (PCA): PCA seeks a linear combination ofvariables such that the maximum variance is extracted from the variables.It then removes this variance and seeks a second linear combination whichexplains the maximum proportion of the remaining variance, and so on.This is called the principal axis method and results in orthogonal(uncorrelated) factors. PCA analyzes total (common and unique) variance

- Dimensionality : It is the number of random variables in a dataset or simply the number of features, or rather more simply, the number of columns present in your dataset.
- Correlation It shows how strongly two variable are related to each other. The value of the same ranges for -1 to +1. Positive indicates that when one variable increases, the other increases as well, while negative indicates the other decreases on increasing the former. And the modulus value of indicates the strength of relation.

- Orthogonal: Uncorrelated to each other, i.e., correlation between any pair of variables is 0.
- They represent the directions in which the data has maximum variance and also the directions in which the data is most spread out. If we are given a large dataset with multiple features, in which it would be difficult to select which of the variables (features) are the most important in determining the target, this PCA plays a huge role.

Why pca is great ?

- PCA reduces attribute space from a larger number ofvariables to a smaller number of factors and as such is a"non-dependent" procedure (that is, it does not assume adependent variable is specified).• PCA is a dimensionality reduction or data compressionmethod. The goal is dimension reduction and there is noguarantee that the dimensions are interpretable •To select a subset of variables from a larger set, basedon which original variables have the highest correlationswith the principal component.

- Thus, PCA is a method that brings together:A measure of how each variable is associated with one another. (Covariance matrix.)The directions in which our data are dispersed. (Eigenvectors.)The relative importance of these different directions. (Eigenvalues.)PCA combines our predictors and allows us to drop the Eigenvectors that are relatively unimportant.

referances

https://arxiv.org/ftp/arxiv/papers/1210/1210.5779.pdf

I applied the same methodology with this study.

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