Quantitative biomarkers for human diseases: from collective cell order, spatio-temporal dynamics, to modeling

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Human diseases are associated with massive modifications of genomic, transcriptomic and proteomic signatures of the cells, which result in various pathological phenotypes. However, it is non-trivial to connect different levels of disorder to phenotypes, because a change in the expression of gene or protein (input) triggers many downstream processes and the resulting phenotypes (output). The same is true for the treatment with clinical agents. A target inhibitor often affects more than one pathyways, resulting in unknown side effects.

To date, the output is mostly assessed either by the pathological image analysis or by the high throughput imaging pipline, both of which are shedding light on visual information, such as polymorphism of cells and tissues and expression of proteins by multicolor staining, of fixed, stained samples. The non-invasive phenotyping of living cells and tissues with numerical indices is a promising strategy to extract quantitative biomarkers for human diseases, because such biomarkers are fully complementary to the "static" phenotypes with no crosstalk of information.

In my talk, I will introduce two types of quantitative biomarkers we developed: (A) biomarkers for the quality assessment of human corneal endothelial cells both in vitro and in vivo ^{1,2}, and (B) biomarkers for the discrimination of clinical agents used in the treatment of acute myeloid leukemia patients ^{3,4}.

- 1. Yamamoto, A., Tanaka, H., Toda, M., Sotozono, C., Hamuro, J., Kinoshita, S., Ueno, M., and Tanaka, M. (2019). A physical biomarker of the quality of cultured corneal endothelial cells and of the long-term prognosis of corneal restoration in patients. Nature Biomedical Engineering *3*, 953-960. 10.1038/s41551-019-0429-9.
- Ueno, M., Toda, M., Numa, K., Tanaka, H., Imai, K., Bush, J., Teramukai, S., Okumura, N., Koizumi, N., Yamamoto, A., et al. (2022). Superiority of Mature Differentiated Cultured Human Corneal Endothelial Cell Injection Therapy for Corneal Endothelial Failure. American Journal of Ophthalmology 237, 267-277. <u>https://doi.org/10.1016/j.ajo.2021.11.012</u>.
- Monzel, C., Becker, A.S., Saffrich, R., Wuchter, P., Eckstein, V., Ho, A.D., and Tanaka, M. (2018). Dynamic cellular phenotyping defines specific mobilization mechanisms of human hematopoietic stem and progenitor cells induced by SDF1α versus synthetic agents. Scientific Reports *8*, 1841. 10.1038/s41598-018-19557-x.
- 4. Ohta, T., Monzel, C., Becker, A.S., Ho, A.D., and Tanaka, M. (2018). Simple Physical Model Unravels Influences of Chemokine on Shape Deformation and Migration of Human Hematopoietic Stem Cells. Scientific Reports *8*, 10630. 10.1038/s41598-018-28750-x.