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Deep learning predicts the differentiation of kidney organoids derived from human induced pluripotent stem cells

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Objectives: Kidney organoids derived from human pluripotent stem cells (hPSCs) contain multi-lineage nephrogenic progenitor cells and can recapitulate the development of the kidney. Kidney organoids derived from hPSCs have the potential to be applied in regenerative medicine as well as renal diseases modeling, drug screening, and nephrotoxicity testing. Despite biotechnological advances, individual differences in morphological and growth characteristics among kidney organoids need to be addressed before clinical and commercial application. In this study, we hypothesized that an automated non-invasive method based on deep learning of bright-field images of kidney organoids can predict their differentiation status.

Methods: Bright-field images of kidney organoids were collected on day 18 after differentiation. To train the convolutional neural networks (CNNs), we utilized a transfer learning approach: CNNs were trained to predict the differentiation of kidney organoids on bright-field images, based on the mRNA gene expression of renal tubular epithelial cells as well as podocytes.

Results: The best-performing prediction model with DenseNet121 had a total Pearson correlation coefficient score of 0.783 on a test dataset. Furthermore, we focused on the classification of kidney organoids into two categories: organoids with above-average gene expression (*Positive*) and those with below-average gene expression (*Negative*). Comparing the best-performing CNN with human-based classifiers, the CNN algorithm had a receiver operating characteristic-area under the curve (AUC) score of 0.85, while the experts had AUC score of 0.48. Time needed to classify organoids by the experts took 1.04 seconds, but 0.014 seconds by CNN.

Conclusions: These results confirmed our original hypothesis and demonstrate that our artificial intelligence algorithm can successfully recognize the differentiation status of kidney organoids.