Docket #: S22-495

Deriving human induced pluripotent stem cells from pre-exposed fibroblasts

Researchers at Stanford have created human induced pluripotent stem cells (hiPSCs) derived from adult human dermal fibroblasts exposed to an environmental factor. In proof-of-concept studies, they were exposed to polystyrene (PS), one of the most commonly used plastics and environmental pollutants. Plastic pollution is increasing at an alarming rate, yet the impact of this pollution on human health is poorly understood. Since skin is the most frequently used source for derivation of hiPSCs and in direct contact with pollutants, hiPSCs derived from dermal fibroblasts offer a powerful platform to start to identify molecular biomarkers of environmental pollution in human cells.

Adult human dermal fibroblasts, used for their reprogramming and derivation of hiPSCs, were exposed to PS. The genetic and epigenetic profiles of both exposed fibroblasts and derived hiPSC were studied, revealing commonly altered genes, signaling circuits, and pathways involved in human diseases. Even when exposed to a low concentration of PS, hiPSCs demonstrated altered DNA methylation and transcriptomic profiles. This strategy for deriving new hiPSC lines can help define the impact of epigenetic memory/mechanisms and environmental pollution on human health, identifying specific cellular responses, and narrowing down the list of candidate biomarkers. The derived cell lines can thus help to decipher the origins of environment-related diseases and offer new therapeutic targets.

This strategy can also be applied to study or test new drugs, cosmetic products, chemicals, or any other exposure factor, not just environmental pollutants. It can be used to establish a cell bank that will supply researchers (environmental investigators, clinicians, drug developers) with fibroblasts or cells of other origin pre-exposed to different factors and the derived hiPSCs. Derived new hiPSC lines and

differentiated hiPSCs can also be retained and offered for further and more accurate studies.

Stage of Development
Proof of Concept

Applications

- Cellular models to identify genetic and epigenetic alterations and changes in signaling circuits associated with exposure to environmental pollutants, new chemicals, and drugs
- Cellular models to identify therapeutic targets and biomarkers for human diseases associated with exposure to the above-described factors
- Cell bank of exposure models as described above

Advantages

- New model/strategy for the study of environmental and other exposure impacts on the cellular level
- Ability to narrow down and prioritize biomarkers of human health related to the exposure/environment
- Ability to illuminate therapeutic targets for environment-related diseases

Publications

- Miodrag Stojkovic, Francisco Manuel Ortuño Guzmán, Dongjun Han, Petra Stojkovic, Joaquin Dopazo, Konstantina M. Stankovic. Polystyrene nanoplastics affect transcriptomic and epigenomic signatures of human fibroblasts and derived induced pluripotent stem cells: Implications for human health. *Environmental Pollution*. Volume 320 (2023).

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