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Blood test predicts insulin resistance using an iPSC (induced pluripotent stem cell) model

Stanford researchers have formulated a risk scoring calculator using a human induced pluripotent stem cell (iPSC) model to accurately predict and calculate insulin resistance via a novel blood test. This allows insight into potential critical early intervention of diabetic and cardiovascular events. Since endothelial dysfunction precedes the onset of obstructive coronary disease and type 2 diabetes mellitus (T2DM) has a strong correlation with cardiovascular disease, inventors studied the patient-specific molecular signatures of iPSC-derived endothelial cells (iPSC-ECs). With this vital information, more precise and targeted clinical management is possible before complications (such as endothelial dysfunction and subsequent atherosclerosis) arise.

Phenotypic differences in iPSC-ECs are likely due to single nucleotide polymorphisms (SNPs) and not the environment. Hence, this method predicts the risk of developing insulin resistance through genetics alone. For example, South Asians have a higher prevalence of insulin resistance, diabetes and cardiovascular disease when compared to Europeans of similar age. Data from the U.K. with European and South Asians with similar Western diet and lifestyle suggested a genetic predisposition.

Several critical challenges were solved by this discovery. First, this system was proven to be easier to use, less invasive, and less cumbersome with more predictive value compared to current methods. Secondly, the invention fulfills a large unmet medical need as the cause of insulin resistance and how it impacts the vascular system is not fully understood and there is a dire need for early diagnostic strategies. Finally, there are limited drug therapies available. Diet, exercise and anti-diabetic medications are currently the only evidence-based therapies for insulin resistance. Research into SNPs will provide further insight into novel drug therapies

and can act as a platform for future discoveries.

The expansive number of individuals this risk scoring calculator may reach is astounding. According to Medscape, T2DM rates have quadrupled worldwide since 1980. Moreover, the World Health Organization (WHO) states that 17.9 million people die each year from cardiovascular disease, an estimated 31% of all deaths in the world. This innovative framework can very well prevent the emergence of an imminent health crisis.

Stage of Development:

Inventors measured the levels of one or more insulin resistance biomarkers from iPSCs derived from somatic cells of the individual. These iPSCs were differentiated into iPSC-ECs. Then, researchers determined whether the iPSC-ECs obtained from a patient were insulin-resistant or insulin-sensitive.

Further ongoing research may be dedicated to the identification and characterization of SNPs that cause insulin resistance and cardiovascular disease, thus refining even more accurate and precise risk calculators.

Applications

- **Early and novel therapeutic and diagnostic strategies** for diabetes and cardiovascular disease patients

Advantages

- **Easier clinical use, less invasive, less cumbersome and more predictive value** compared to current methods
    - The gold standard in research, euglycemic insulin clamp, is unwieldy in a clinical setting
    - The oral glucose challenge and Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) are also time consuming and not as accurate as the euglycemic clamp
    - Current tests require an individual to manifest insulin resistance
- **Prevents significant morbidity and mortality**

- **Hones-in on genetic makeup**

Patents

- Published Application: WO2021021649
- Published Application: 20220273591

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