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# Functional Assessment of the Induced Pluripotent Stem Cells (iPSC)-derived β-like Cells

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## Background and Aim

**Human β-like cells (BLCs)** derived from **induced Pluripotent Stem Cells (iPSC)** are an emerging tool to study human **β-cell development and function**.

We established a **functional assessment** of each of our differentiation on the following properties:

- **Secretory response** (insulin secretion assay)
- **Exocytosis kinetics** (capacitance measurement)
- **Ultrastructure** (Electron microscopy)
- **β-cells electrical coupling** (Multi-Electrode Array, MEA)

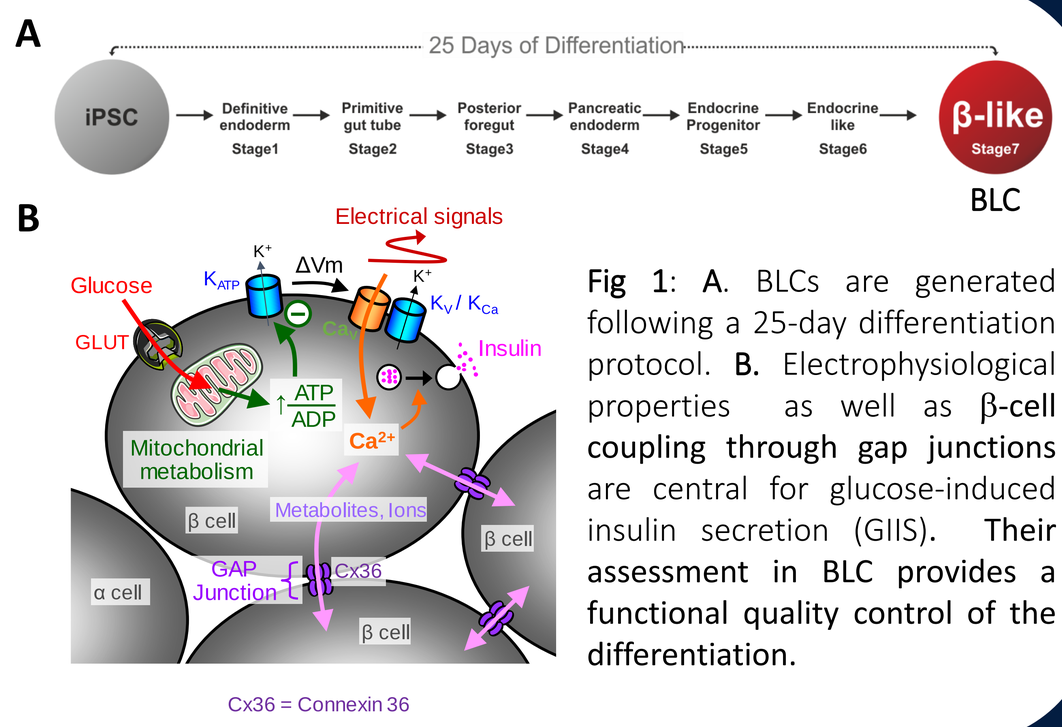


**Fig 1**: **A.** BLCs are generated following a 25-day differentiation protocol. **B.** Electrophysiological properties as well as β-cell coupling through gap junctions are central for glucose-induced insulin secretion (GIIS). Their assessment in BLC provides a functional quality control of the differentiation.

## Results

### Secretory response

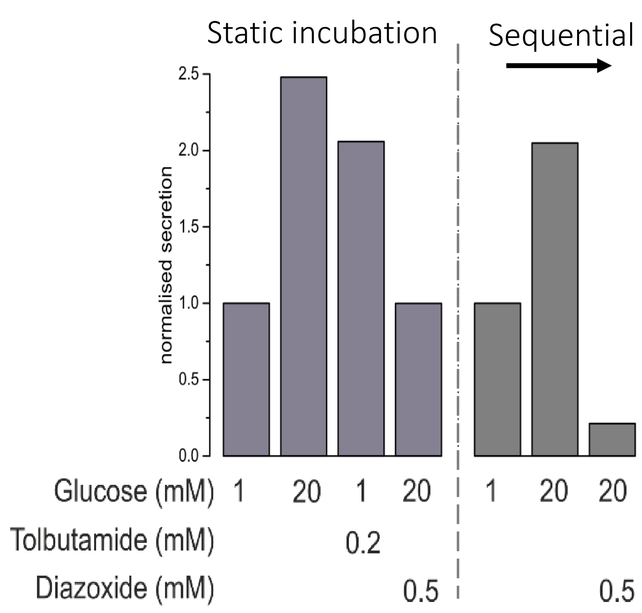


**Fig 2**: Representative GIIS induced by 1 and 20mM glucose and modulators of $K_{ATP}$ channels activity (Tolbutamide/Diazoxide). The stimulations are either parallel static incubations (left), or sequential on the same BLC preparation (right).

### Electrical activity and exocytosis (single-cell)

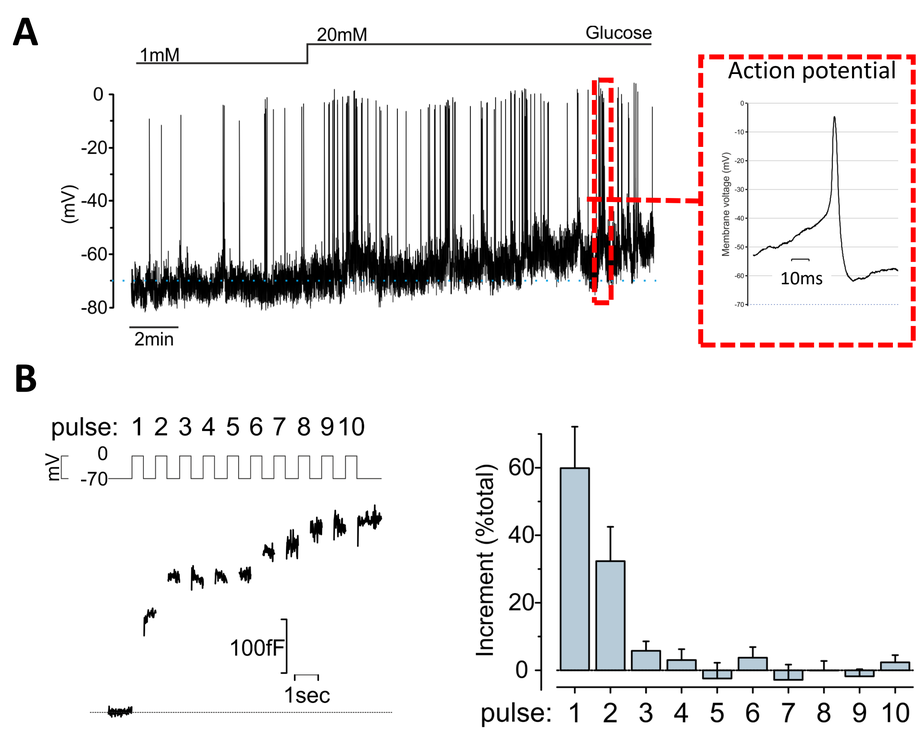


**Fig 3**: **A.** Glucose stimulation triggers action potential firing (n=3 cells). Action potential kinetics is similar to human primary β-cells (10ms duration). **B.** Exocytosis triggered by a train of 10 depolarisations to 0mV is biphasic as in human primary β-cells (Raw trace left, quantification right, n=7 cells).

### Ultra structure

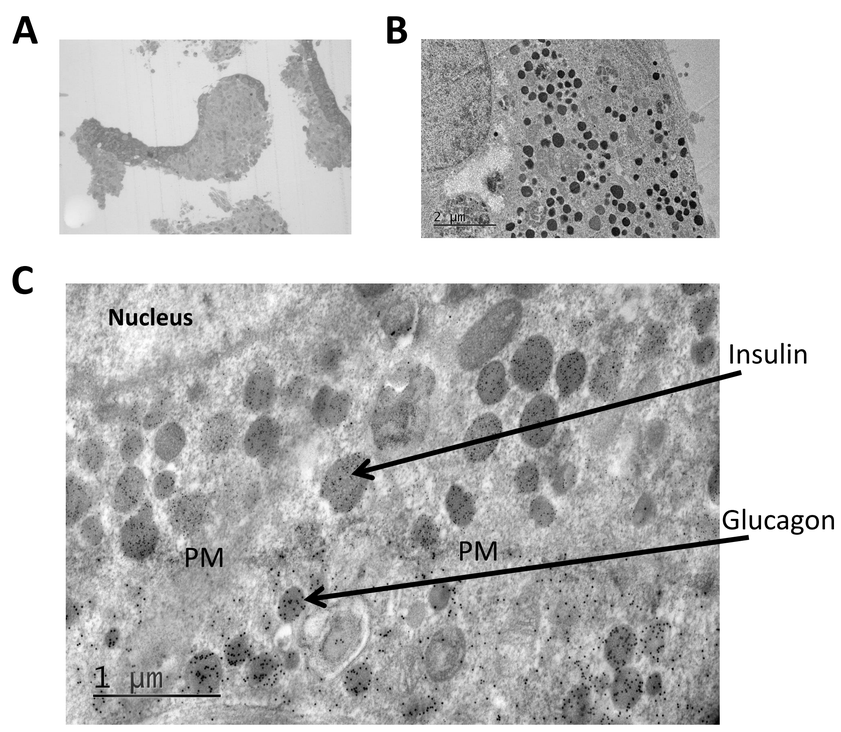


**Fig 4**: **A.** Semi thin section showing cell heterogeneity. **B.** Ultra structure of BLC. Scale bar: 2µm **C.** Immunogold labelling of insulin (BLC, 10nm gold particles, top) and glucagon (15nm gold particle, alpha-like cell, bottom). PM: Plasma Membrane. Scale bar: 1µm.

### Multicellular activity assessed by MEA and its automatic analysis in hard real-time

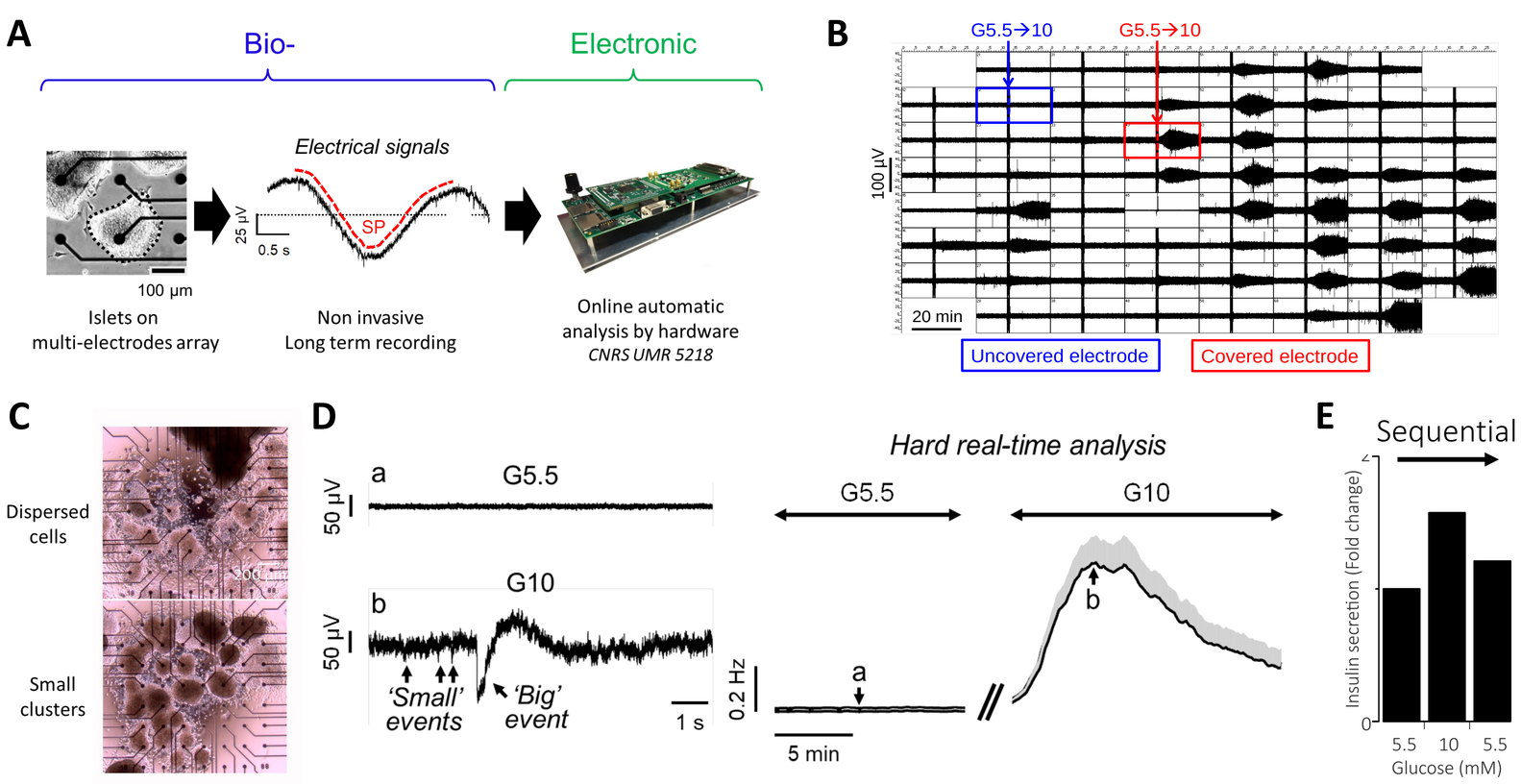


**Fig 5**: **A.** Principle of the approach: islets on MEA generate slow potentials (SP) analysed by a microelectronic circuit. SPs are β cell-specific coupling signals. **B.** 60 recording channels showing β-like cells activity. **C.** Images of preparations. **D.** Representative traces at 5.5 and 10mM glucose and real-time analysis of SP frequencies (means+SEM, n= 29 electrodes). **E.** Corresponding insulin secretions.

## Conclusions

**β-like cells** derived from **iPSC** exhibit critical human β-cell features:

- Glucose-induced insulin secretion
- Electrical excitability and exocytosis
- Electrical coupling

BLCs allow functional studies on human β-cell differentiation. The emergence of new differentiation protocols should improve their homogeneity and ultrastructure.

This pipeline will support the characterization of T2D-risk alleles on human β-cell function.

University of Oxford · université de Bordeaux · cbmn · ims · MRC Medical Research Council · EFSD European Foundation for the Study of Diabetes · wellcome