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Neurons Derived From P19 Embryonic Carcinoma Cells As A Platform For Biosensor Applications

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INTRODUCTION: P19 is a mouse-derived embryonal carcinoma cell line capable of differentiation toward ectodermal, mesodermal and endodermal lineages. Cell lines offer advantages of reproducibility, unlimited availability, homogeneity and pliability to genetic manipulation. A spontaneously active neuronal ensemble derived from differentiated P19 cells cultured on microelectrode array can thus be engineered to sense a variety of chemical compounds with the potential to provide sensitivity, accuracy and long term on line performance as a biosensor.

METHODS: Microelectrode arrays (MEA) were purchased from MultiChannel Systems. P19 embryonic carcinoma cells were differentiated into neurons by treating with retinoic acid and cultured up to a month on the MEAs. Immunohistology was performed on the P19-derived neurons. The response of the P19-derived neurons to two major neurotransmitters, γ-aminobutyric acid (GABA) and glutamate, and their antagonists was studied. The cells were tested with different concentration of GABA, bicuculline, musimol, glutamate, cyclothiazide, the 2, 3-bezodiazepine derivative, GYKI 52466 to examine their plausibility as a biosensor. Recordings were done with MC rack software and analysed.

RESULTS: Recordings obtained from the cultures showed consistency within the same batch of differentiated P19 cells. Spontaneous neuronal activity was detected after 7 days *in vitro* (Fig. 1). We found that P19-derived neurons developed network activity with synchronised burst activity after 15 days *in vitro* (Fig. 2). Activity could be detected usually in regions where cell clusters were attached to the electrodes. Synchronised firing patterns were observed in electrodes connected together in the same cell cluster network.

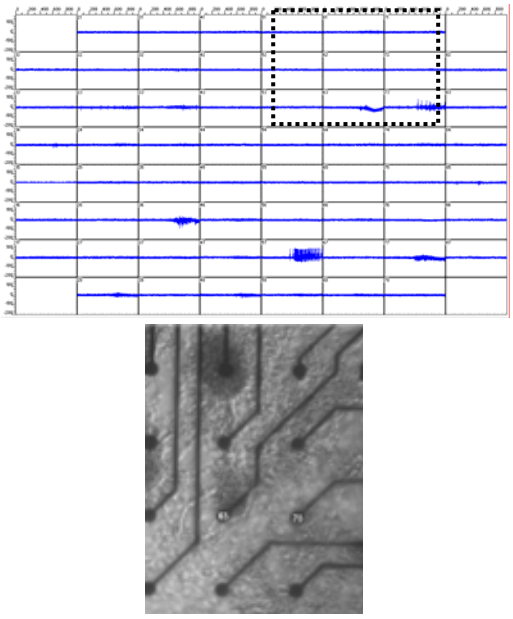

Fig. 1: Intrinsic extracelluar signals of P19-derived neurons after 17 days in vitro. Below: Optical micrographs of the cells at the corresponding electrodes highlighted.

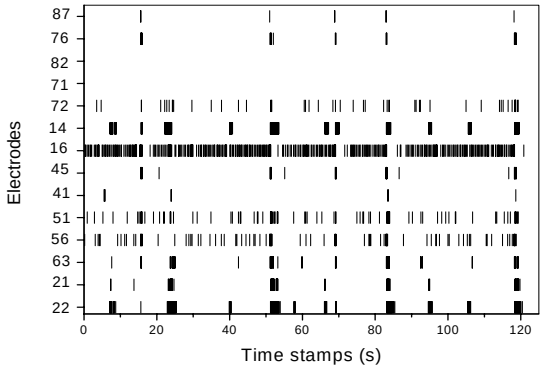

Fig. 2: Raster plots of P19-derived neuronal culture after 23 days in vitro.

DISCUSSION & CONCLUSIONS: P19-derived neurons were able to form network connections displaying network properties. P19-derived neurons appeared to give inhomogenous response to the neurotransmitters exposed. Ongoing work is done at the moment to further analyse their responses.