

**96th Annual Meeting**  
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**Abstract Number:** LB-124

**Presentation Title:** Granulin promotes proliferation and aggregation of differentiating neural progenitors

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**Objective:** Granulin is a growth factor that is over expressed in high-grade gliomas. We have shown that granulin is a potent mitogen for astrocytes and glioblastoma cells; however, the cellular substrate for granulin is unknown. The objective of our work was to examine the role of granulin in neural progenitor proliferation. Our first hypothesis was that granulin is an autocrine-paracrine growth factor that is released from neural progenitors. Our second hypothesis was that granulin promotes proliferation of differentiating neural progenitors.

**Methods:** To test our first hypothesis, we cultured dissociated neural progenitors on poly-L-lysine coated glass cover slips and incubated them with antibodies to granulin and nestin. These cells were then labeled with fluorescent secondary antibodies and examined using video microscopy. To address our second hypothesis, we subcultured dissociated neurospheres in a differentiation medium containing neurobasal medium and retinoic acid (DM). The first group was a control group cultured in DM alone. The second group was cultured in a DM with granulin (GRN) at a concentration of 100 µg/ml. The third group was cultured in DM and 1:100 dilution of granulin antibody (GRNAB). These cells were maintained in these conditions, with the cells being fed appropriate concentrations of either granulin peptide or granulin antibody each day. After five days, the diameter and number of cell aggregates were recorded.

**Results:** After immunolabeling, we found a population of cells that were strongly positive for both granulin and nestin, indicating co-expression of these molecules in neural progenitors. The results of our cell proliferation studies were as follows (mean number of cell aggregates per well) control (33); GRN (44.3), GRNAB (55.7); cell diameter measurements (mean µm ± standard deviation µm) control (56.4 ± 23.3), GRN (88.9 ± 40.4), GRNAB (58.4 ± 21.8).

**Conclusion:** We have identified a sub-population of nestin-positive, granulin-positive neural progenitors. Application of granulin to differentiating neural progenitors results in cellular proliferation and aggregation of proliferating progenitors. Blockade of granulin activity prevents formation of cellular aggregates and attenuates proliferation. These data suggest that granulin plays an important role in controlling neural progenitor proliferation. Studies are currently underway to validate these findings and to further examine the role of granulin in neural progenitor proliferation and differentiation.

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