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Current Research

Owing to their oncotropic and oncolytic properties, parvovirus-based vectors represent interesting candidates for anti-tumour therapy in the brain. Viral vectors must fulfil an important criterion for a safe therapeutic use, i.e. their specific targeting at neoplastic cells, and, if possible, their lack of interference with the host anti-tumour defense. We could show that parvovirus is innocuous to non transformed glial cells and does not interfere with their immune potential.

Microglia, the brain resident macrophages, can efficiently participate in immune responses if appropriately activated. The actual role of microglia in glioma biology remains largely unknown and controversial. *In vitro* and *in vivo* observations suggest that these phagocytes are endowed with tumour-promoting as well as with tumour-destructive capacities. *In vivo*, the ability of glioma to grow despite of the presence of numerous infiltrating microglia indicates an efficient "silencing" of these cells and goes in line with the known immunosuppressive capacity of glioma. A better understanding of the interactions taking place between tumour cells and microglia would definitely help in designing fully efficient strategies that would be appropriate to the unique environment displayed by the brain. In that regard, the use of viral vectors for local gene therapy directed at glioma cells may help not only to kill tumour cells but also to induce or enhance anti-tumour activities of microglia.

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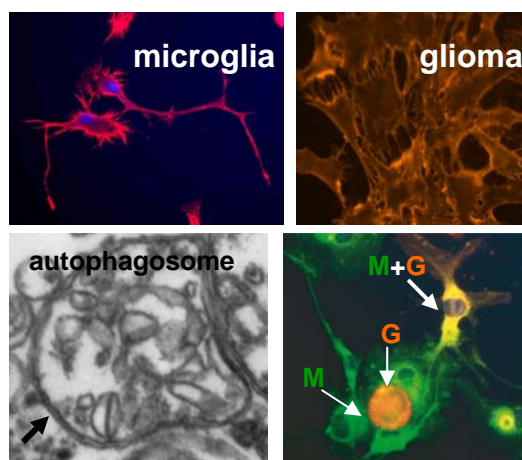
We could show that LPS/IFN- γ activated murine microglia specifically killed glioma cells through autophagy and were able to phagocytose the dying cells. We started to characterise functional interactions between human microglia (cytotoxic and phagocytic activities) and glioma cells (migration, proliferation, immunosuppression).

Future Projects and Goals

- Validation of parvovirus innocuousness *in vivo*
- Identification of the mouse microglial toxic factors
- Identification of the microglia-induced death pathways in glioma cells
- Analysis of pro (migration)-tumour and anti (toxic)-tumour activities of human microglia.

Selected Publications

- Gresser, O., Weber, E., Hellwig, A., Riese, S. and Régnier-Vigouroux, A. (2001) Eur. J. Immunol., 31, 1813-1824.
- Zimmer, H., Riese, S., and Régnier-Vigouroux, A. (2003) Glia, 42, 89-100.
- Abschuetz, A., Kehl, T., Geibig, R., Leuchs, B., Rommelaere, J., and Régnier-Vigouroux, A. (2006) Cell and Tissue Research, 325, 423-436.



Upper left: primary microglia; upper right: glioma cells

Low left: microglia-induced autophagic death in glioma cells

Low right: phagocytosis of dying glioma cells (G) by microglia (M)