

# Robert S. Sawin, M.D.



## • NEUROBLASTOMA IN THE PEDIATRIC PATIENT

### AWARDS

- Robert E. Condon Surgical Resident Competition, 1998
- Wisconsin Surgical Society
  - Resident Competition (Scientific Division), 1998

### FUNDING

- U.S. Army, Madigan Army Medical Center
  - Department of Clinical Investigation

Neuroblastoma is the most common solid malignancy affecting children. Despite treatments involving aggressive regimens of chemotherapy, and even bone marrow transplantation, the mortality for neuroblastoma remains 40 to 50%. The biology of an individual neuroblastoma tumor varies, with advanced stage tumors manifesting very different molecular and genetic features than those with early stage disease.

Perhaps the most intriguing feature of neuroblastoma is the well-documented spontaneous maturation of highly malignant tumors to a more differentiated benign variant, called ganglioneuroma. An understanding of this maturation process, including the molecular signals that trigger that change, might engender therapeutic methods that harness that maturation process.

Our laboratory effort has focused on a particular peptide growth factor, gastrin releasing peptide (GRP),

that is expressed in both adult and pediatric tumors that are derived from neural crest cells. Our work has shown that GRP and its receptor, GRP-R, are both expressed in abundance by neuroblastoma cells in culture and by tumor cells removed from children. Our cell culture studies have also shown that inhibitors of GRP retard neuroblastoma growth.

We are presently working collaboratively with the Clinical Research Institute at Madigan Army Medical Center to define the quantitative differences of GRP and GRP-R expression in neuroblastoma as compared to ganglioneuroma. Our hypothesis is that these differences account for the virulence of the behavior of a given tumor. If verified, this observation would suggest that GRP antagonists might be useful clinically to stimulate maturation of neuroblastoma cells.

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### RELATED PUBLICATIONS

1. Sawin, R.S., Brockenbrough, J. and Ness, J.C. Gastrin releasing peptide is an autocrine growth factor for human neuroblastoma. *Surgical Forum*, 1992; XLIII:606-608.
2. Brockenbrough, J., Ness, J.C. and Sawin, R.S. Scintillation proximity assay accurately quantifies human gastrin releasing peptide. *Life Science News*, 1993; 12:14.
3. Sawin, R.S., Brockenbrough, J. Secretion of Gastrin Releasing Peptide by Retroperitoneal Tumors. *Am J Surgery*, 1995; 169:550-552.
4. Trombetta I, Azarow K, Brown T, Moore K, Sawin R: Telomerase enzyme activity predicts severity of disease in neuroblastoma. *Current Surgery*, 1999; 58:413-416.
5. Sanborn C., O'Connor A., Sawin R.S., Moore K., Dehart M.J., Azarow K.S.: Comparison of telomerase levels before and after differentiation of two cell lines of human neuroblastoma cells. *J Surgical Res*, 2000; 93:206-210.
6. Sebesta JA, Young A, Bullock J, Moore KH, Azarow K, Sawin RS : Gastrin-releasing peptide: a potential growth factor expressed in human neuroblastoma tumors. *Curr Surg*, 2001; 58(1):86-89.

### OTHER CO-INVESTIGATORS

Ken Azarow, M.D.; Madigan Army Medical Center / Ann O'Connor, M.D.; Children's Hospital of Columbus, Ohio

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