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Vascularization of optic gliomas: primitive invertebrate-like channels: Clinical and Therapeutic implications

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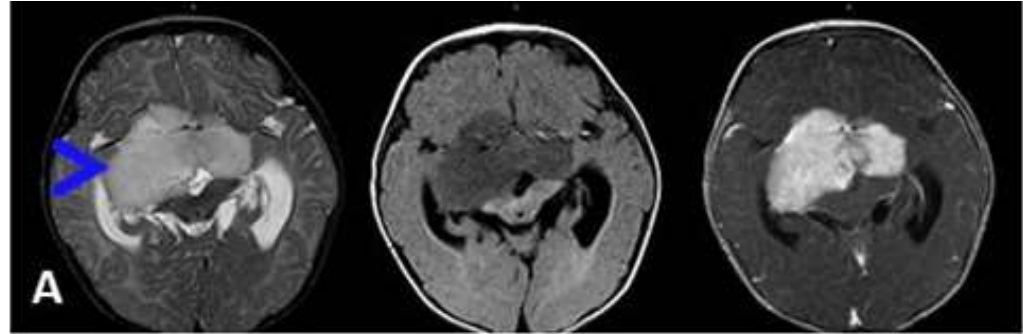
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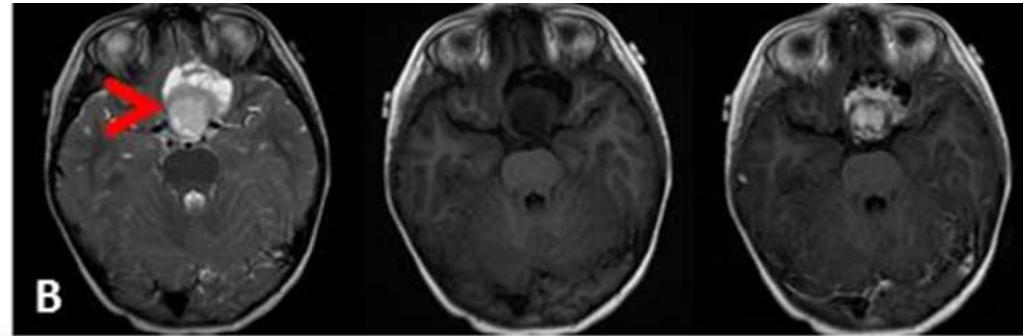
Overview

Optic Pathway Tumors

Pilomyxoid (PMXA)



Pilocytic (PA)



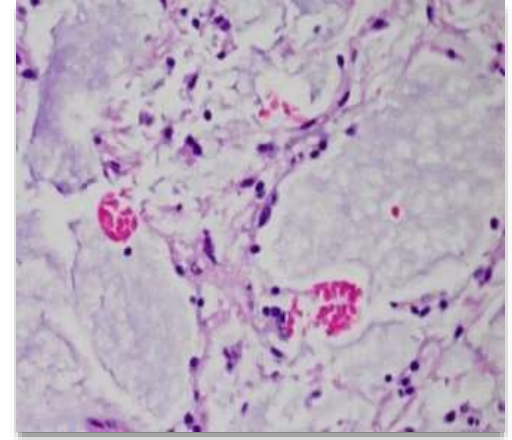
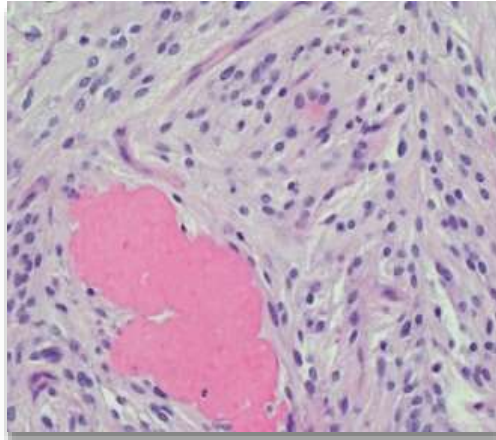
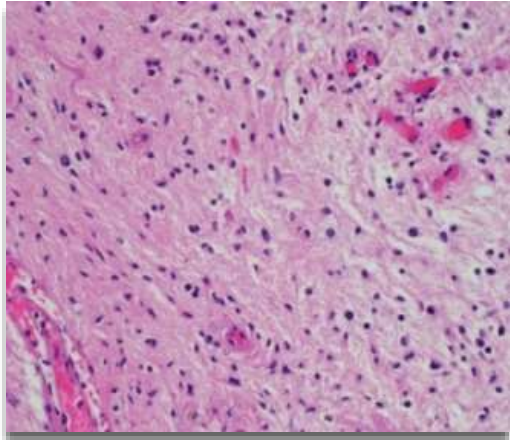
Tumor Angiogenesis

- Hallmark feature of malignancy
- Endothelial cells invariably present
- Endothelial damage leads to thrombosis and cell death
- Target for therapy

Myxoid matrix and Vascularization of OPG

- Myxoid matrix content
 - Versican
 - Hyaluronin and Proteoglycan link protein-1
- Pilomyxoid tumors develop ***endothelium-free*** vascular channels
 - Analogous to invertebrate vascular supply

Pathology

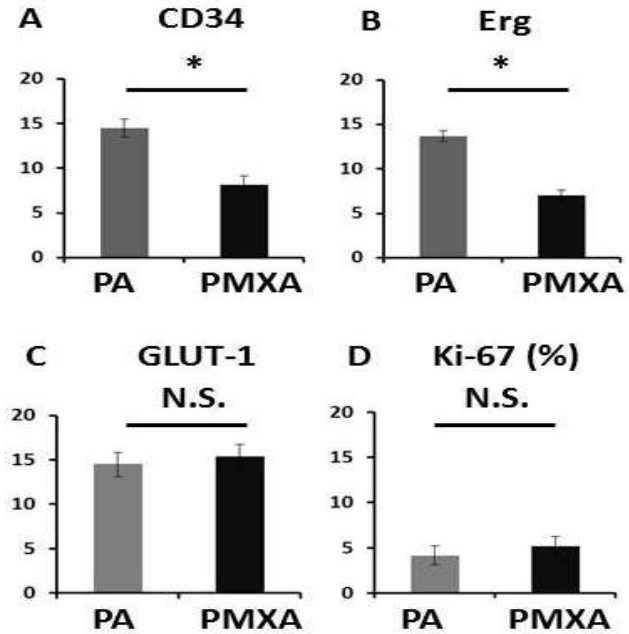


Pilocytic



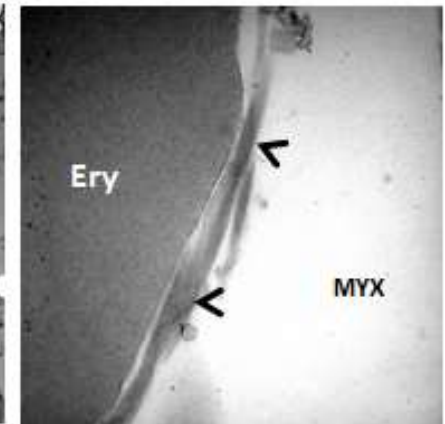
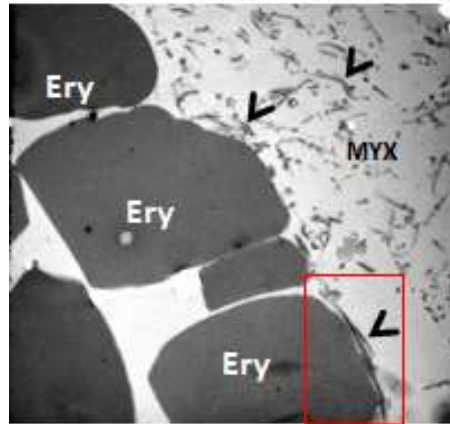
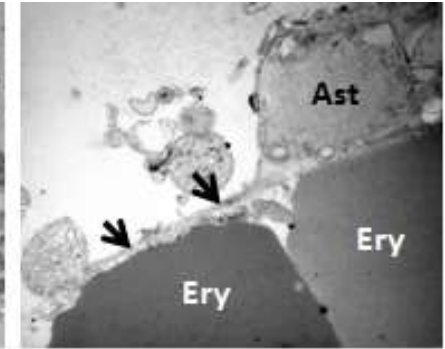
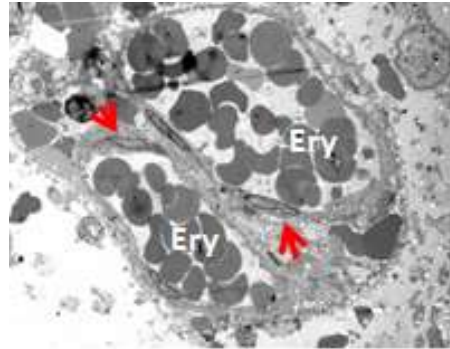
Pilomyxoid

Vascular density

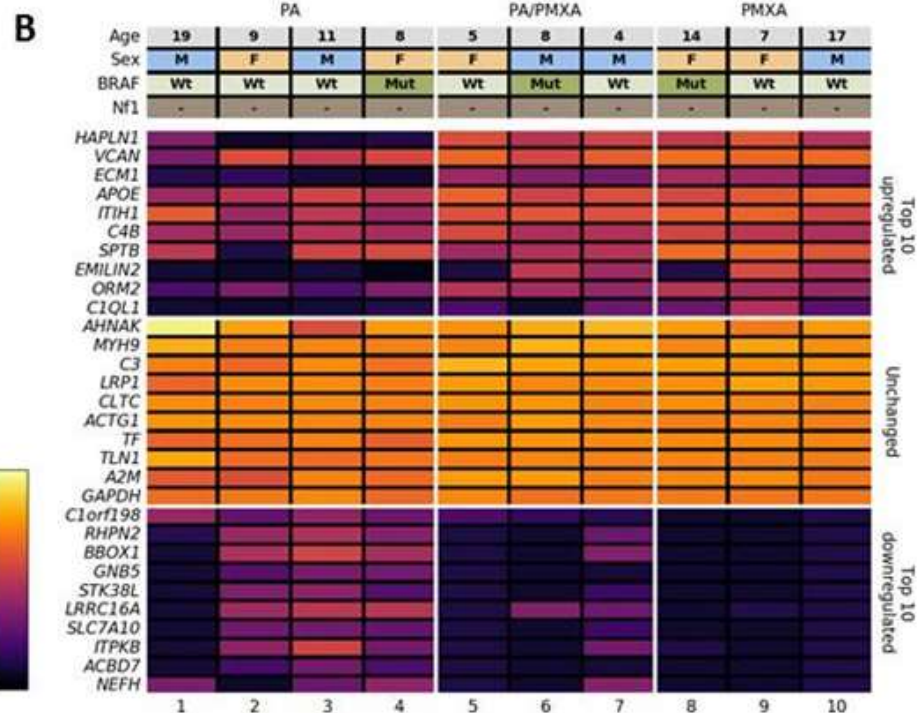
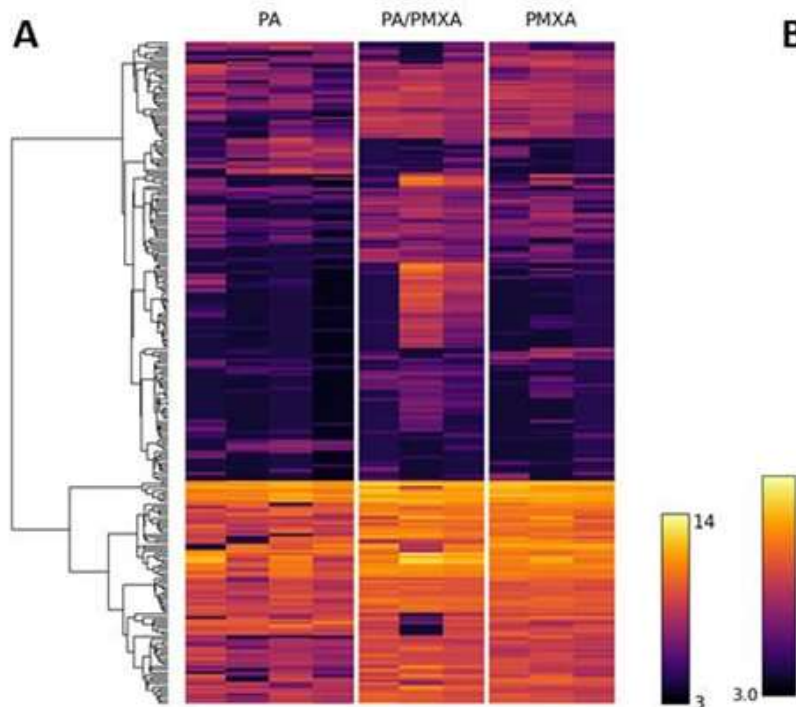


Vascular ultrastructure

- Endothelialized channels
- Astrocyte lined channels
- Direct contact of erythrocytes and myxoid matrix
- Fibrin at interface of erythrocytes and myxoid matrix
- Fibrin absent in between erythrocytes in channels – lack of thrombosis

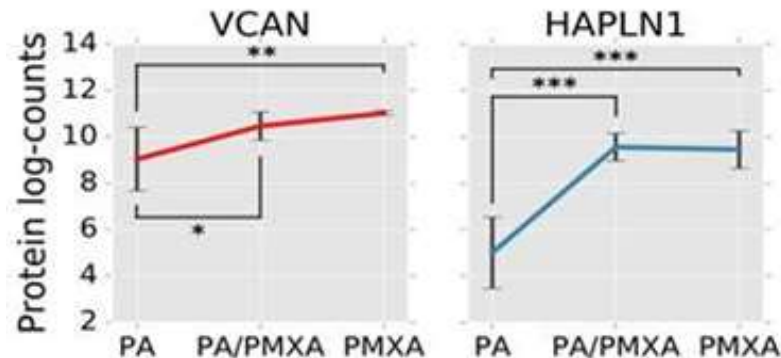


Proteomic analysis



Proteomic analysis

- 5389 Proteins expressed in all tumors
- 188 differentially expressed in three tumor groups
- PMA demonstrated increase in 146, decrease in 42
VCAN (Chondrotin sulfate proteoglycan) 3.7 fold
HAPLN1 (Hyaluronan and Proteoglycan Link Protein 1) 22 fold

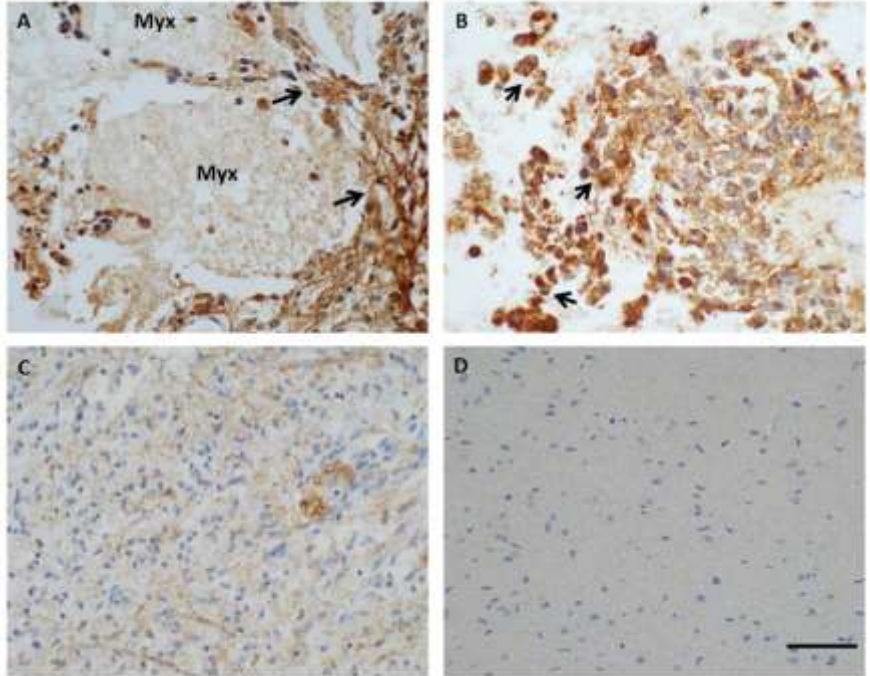


VCAN expression

PMXA – VCAN

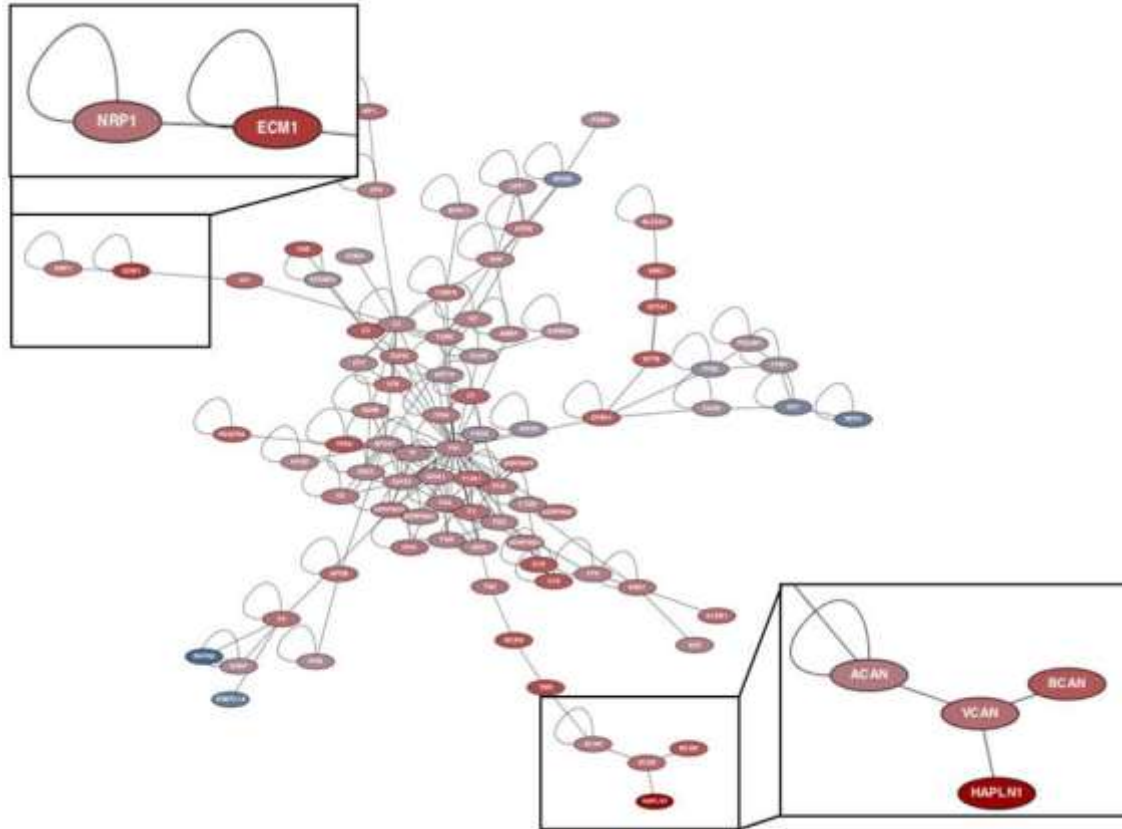
- myxoid matrix
- tumor cells

PA - Sparse VCAN expression



50 micron

Protein-Protein Interactions



Conclusions

- PMA develop vascular channels evocative of invertebrate blood supply
 - Selective metabolic advantage?
- Matrix is composed of VCAN and HAPLAN1
- Potential therapeutic implications:
 - No blood brain barrier
 - Targeting of extracellular matrix

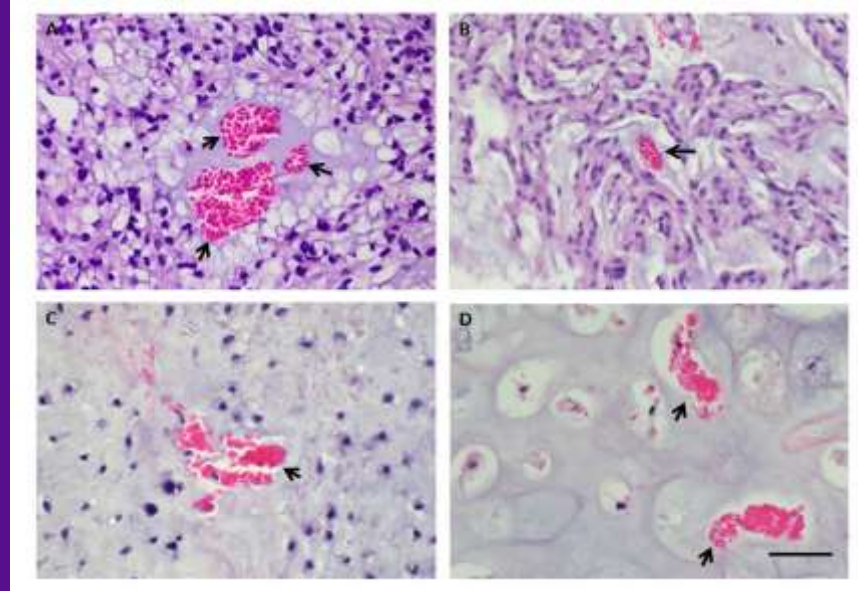
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