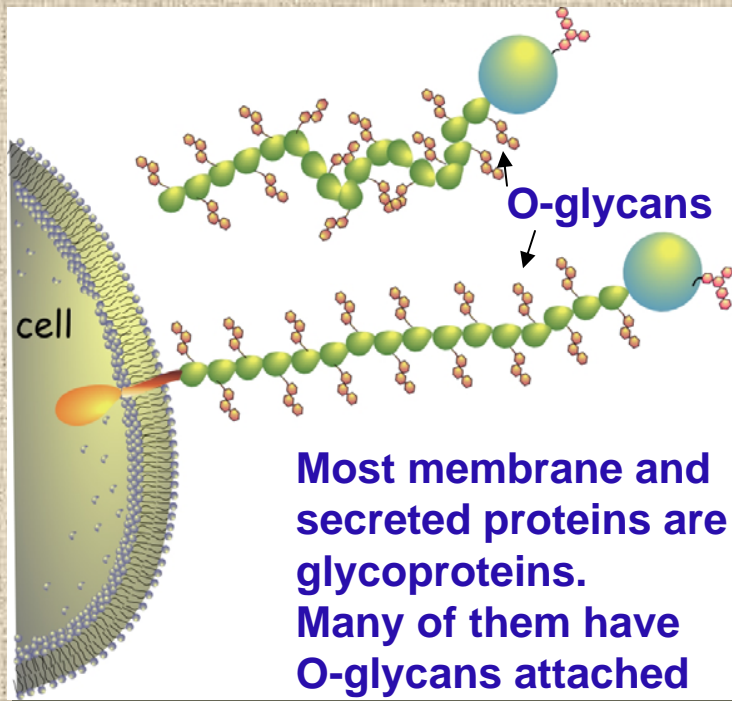


Endothelial O-glycans are essential for angiogenesis

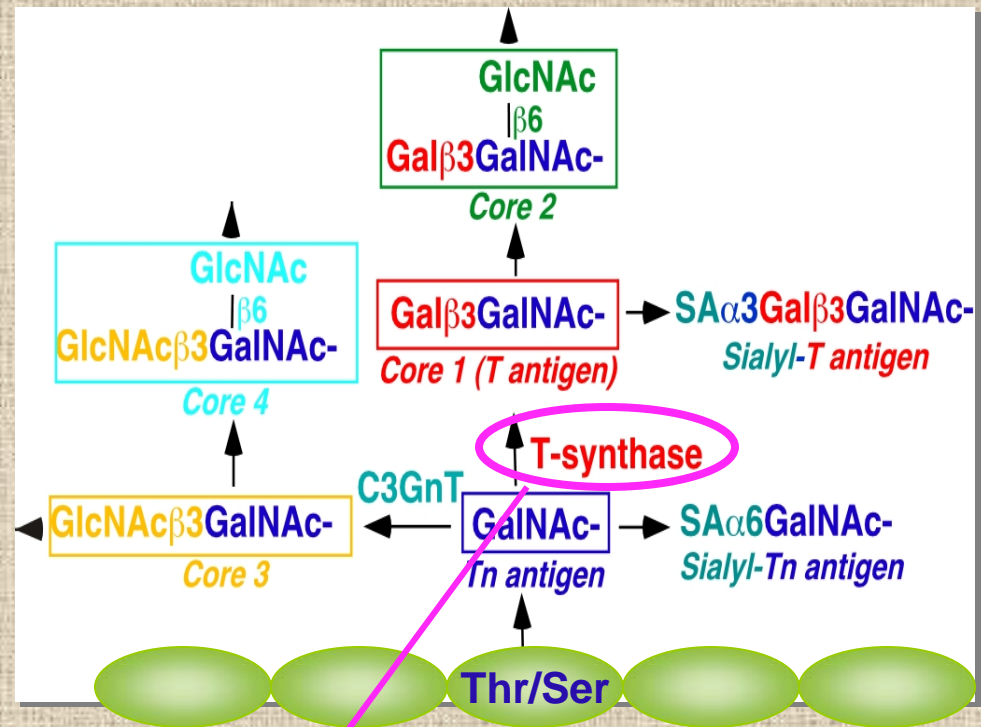
Lijun Xia

**Cardiovascular Biology Research Program
Oklahoma Medical Research Foundation**

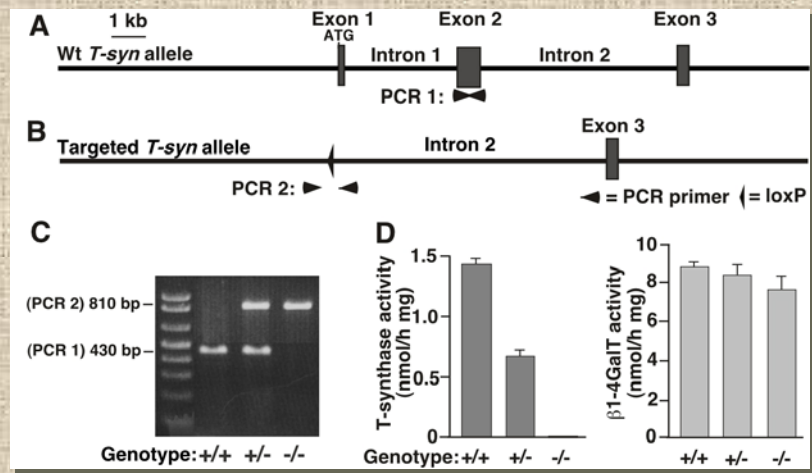
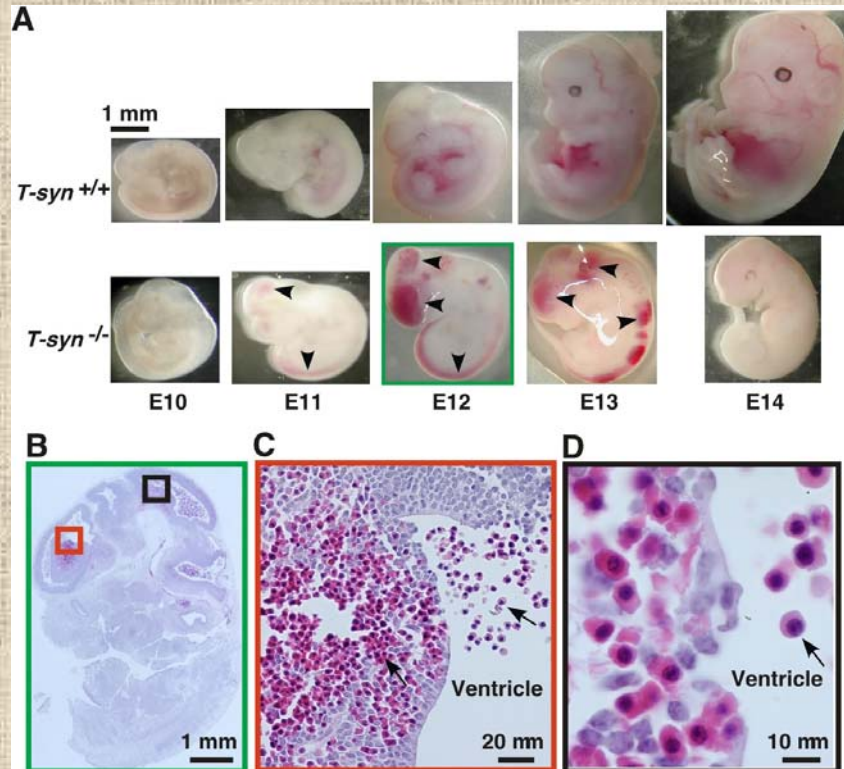




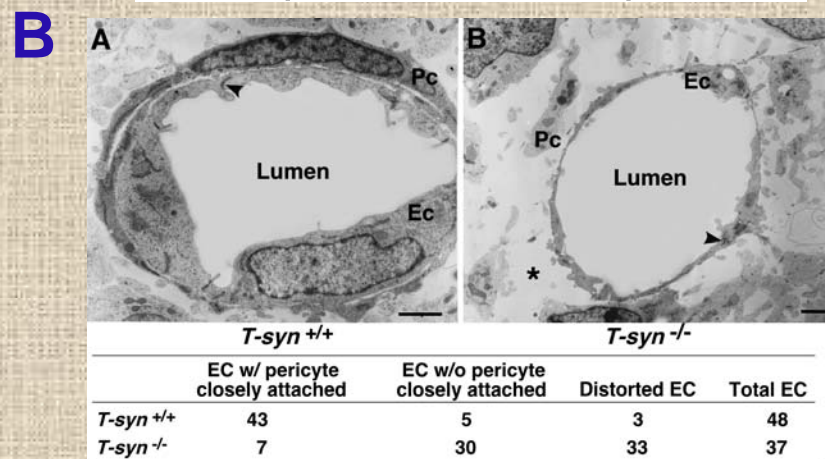
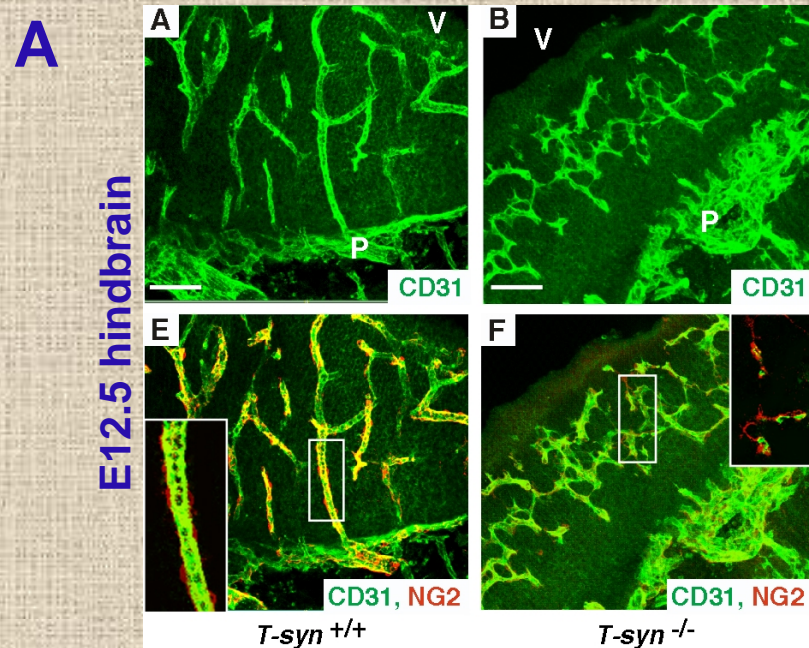
Most membrane and secreted proteins are glycoproteins. Many of them have O-glycans attached



Ju T, et al. Cloning and expression of human core 1β1,3-Galactosyltransferase. *J Bio Chem.* 277:178-186. 2002

A**B**

T-syn^{-/-} mice developed brain/spinal hemorrhage that was fatal by embryonic day 14.

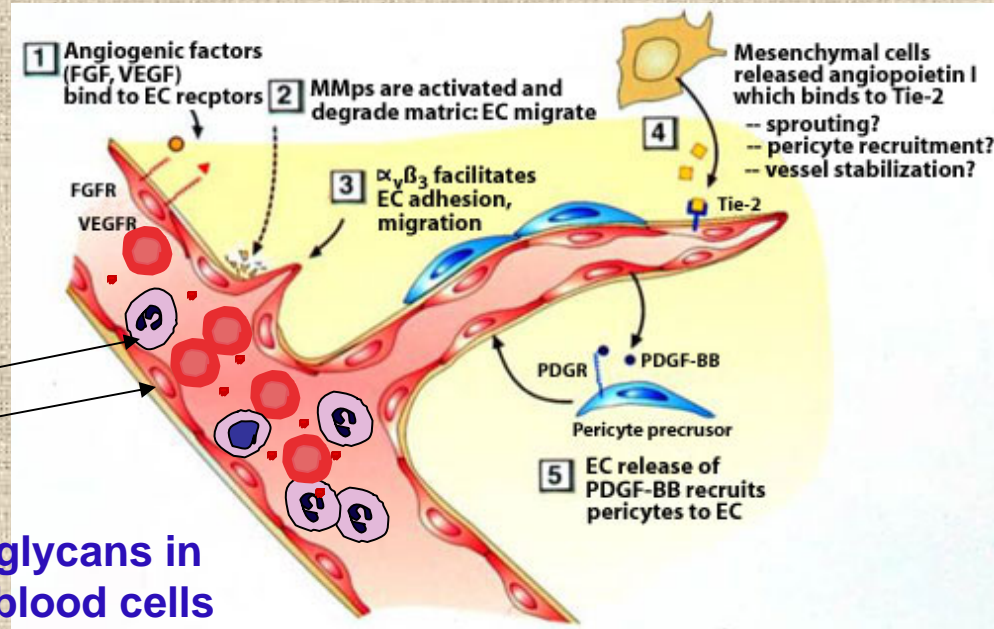
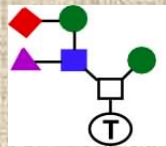


The *T-syn*^{-/-} brains formed a disorganized microvascular network with defective association of endothelial cells with pericytes

Xia L, et al. Defective angiogenesis and fatal embryonic hemorrhage in mice lacking core 1-derived O-glycans. *J Cell Biol.* 164:451-9, 2004.

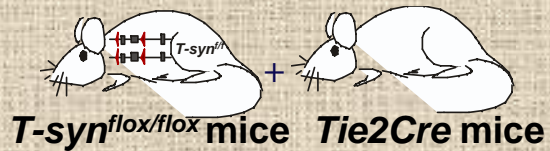
How does the absence of O-glycans cause defective angiogenesis?

- 1. Identify cell types requiring O-glycans for angiogenesis.**
- 2. Elucidate cellular defects and molecular mechanisms.**

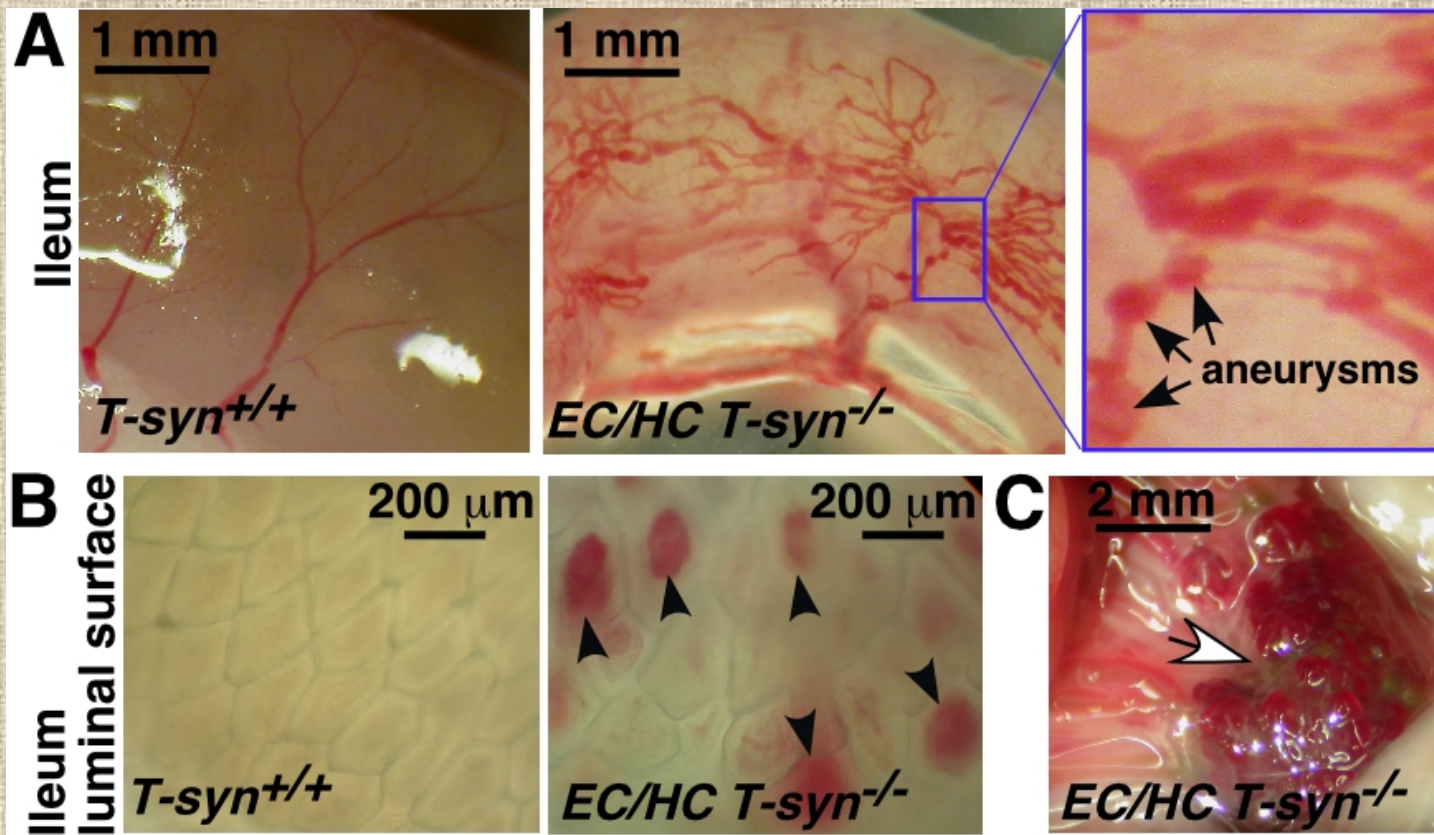


A. Roles of O-glycans in endothelial & blood cells

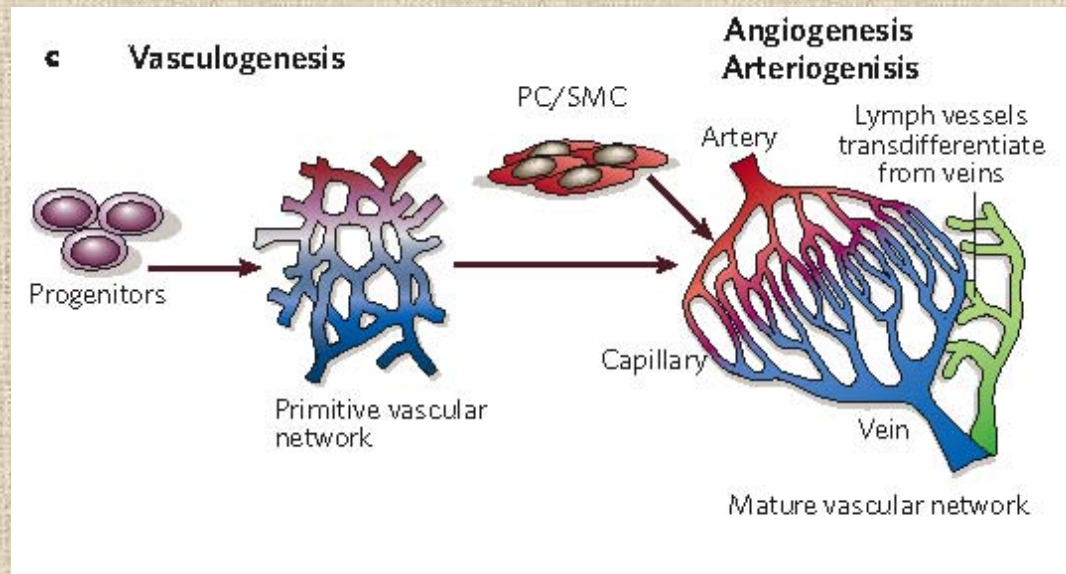
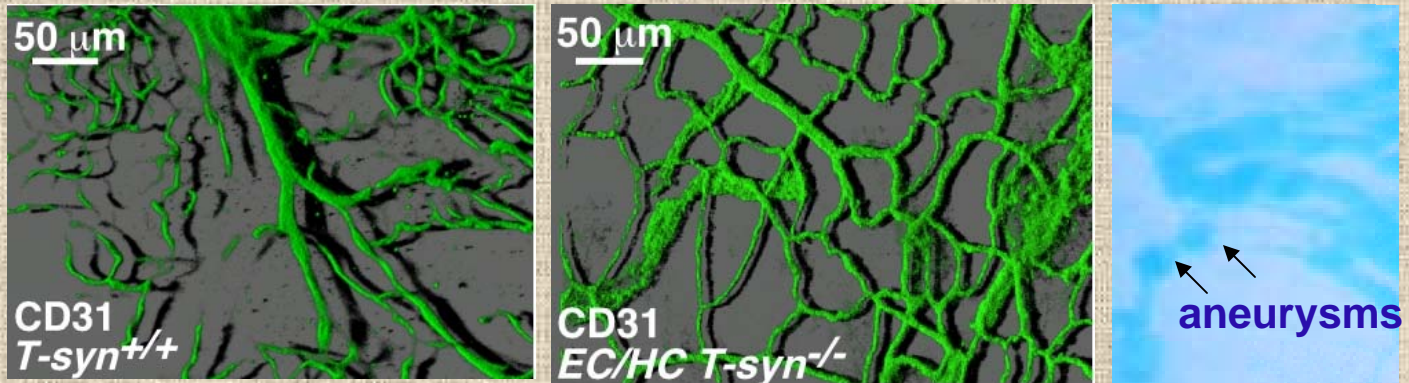
Endothelial & blood cell-specific *T-syn*^{-/-} mice (EC/HC *T-syn*^{-/-})



EC/HC T-syn^{-/-} mice developed highly disorganized vessels with aneurysms



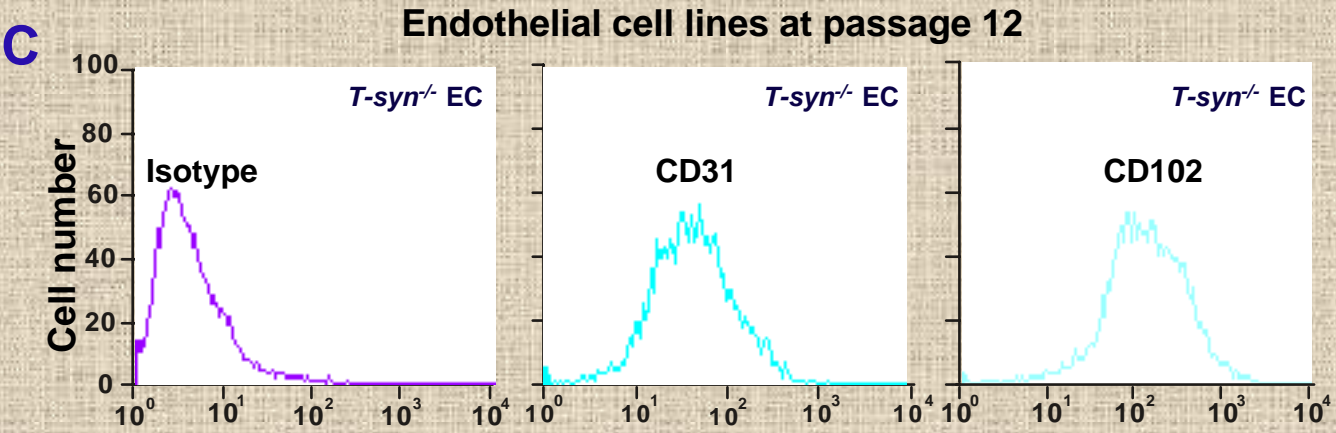
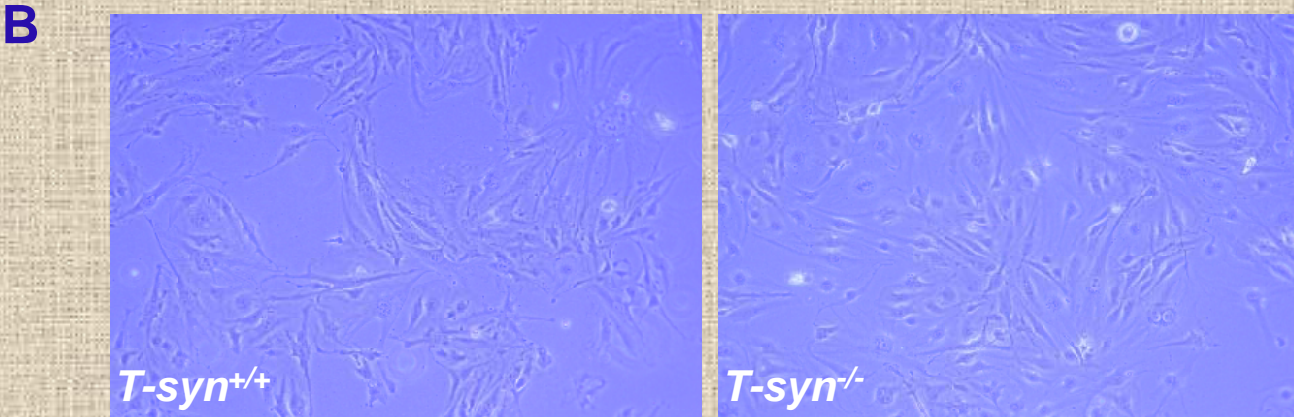
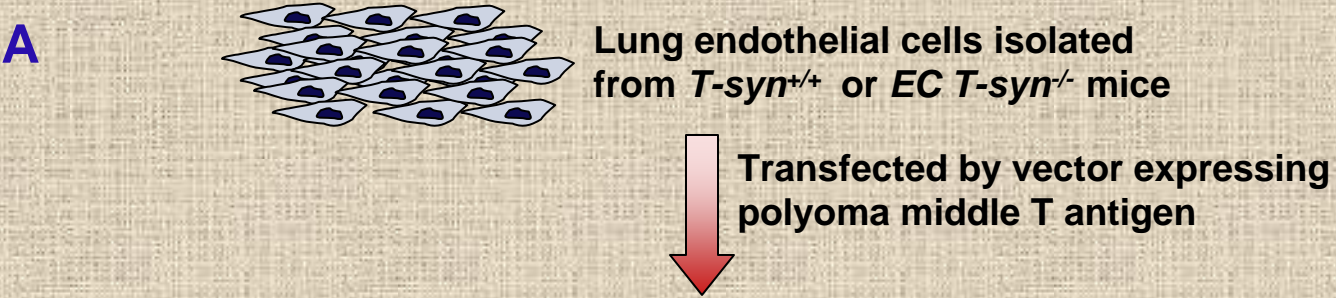
T-syn^{-/-} vessels had defective maturation and remodeling

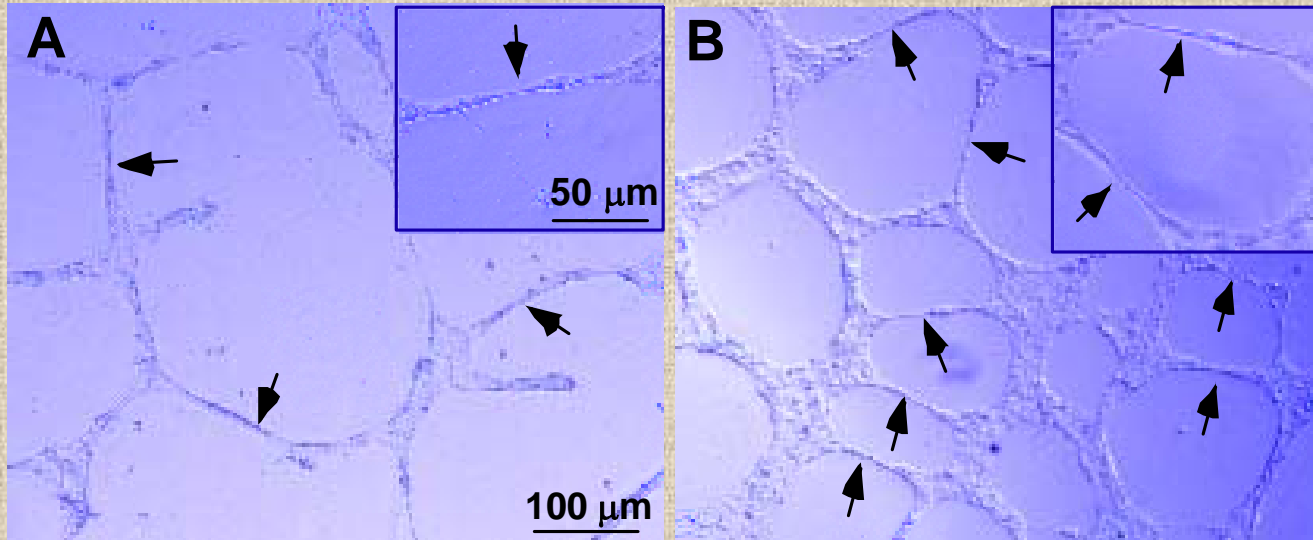


How does the absence of O-glycans cause defective angiogenesis?

1. Identify cell types requiring O-glycans for angiogenesis.
2. Elucidate cellular defects and molecular mechanisms.

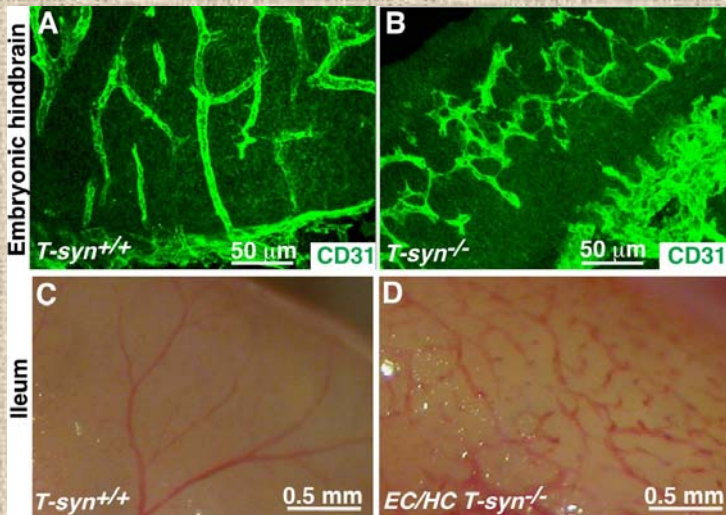
Establish endothelial cell lines





T-syn^{+/+}

T-syn^{-/-}



T-syn^{-/-} endothelial cells formed more tubular structures on Matrigel.

Summary:

- 1. Endothelial core 1-derived O-glycans are essential for angiogenesis.**
- 2. Loss of endothelial core 1-derived O-glycans results in defective vascular remodeling.**
- 3. Altered expression of molecules regulating vascular remodeling is observed in *T-syn*^{-/-} endothelial cells.**