

THE UNIVERSITY OF TEXAS  
MD ANDERSON  
CANCER CENTER

# **Impaired Angiogenesis in Aminopeptidase N-null Mice**

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Arap & Pasqualini Laboratory

# Profiling Cell Surface Markers: Aminopeptidase N (CD13)

**Tumor cell - endothelium**  
cell adhesion and extravasation

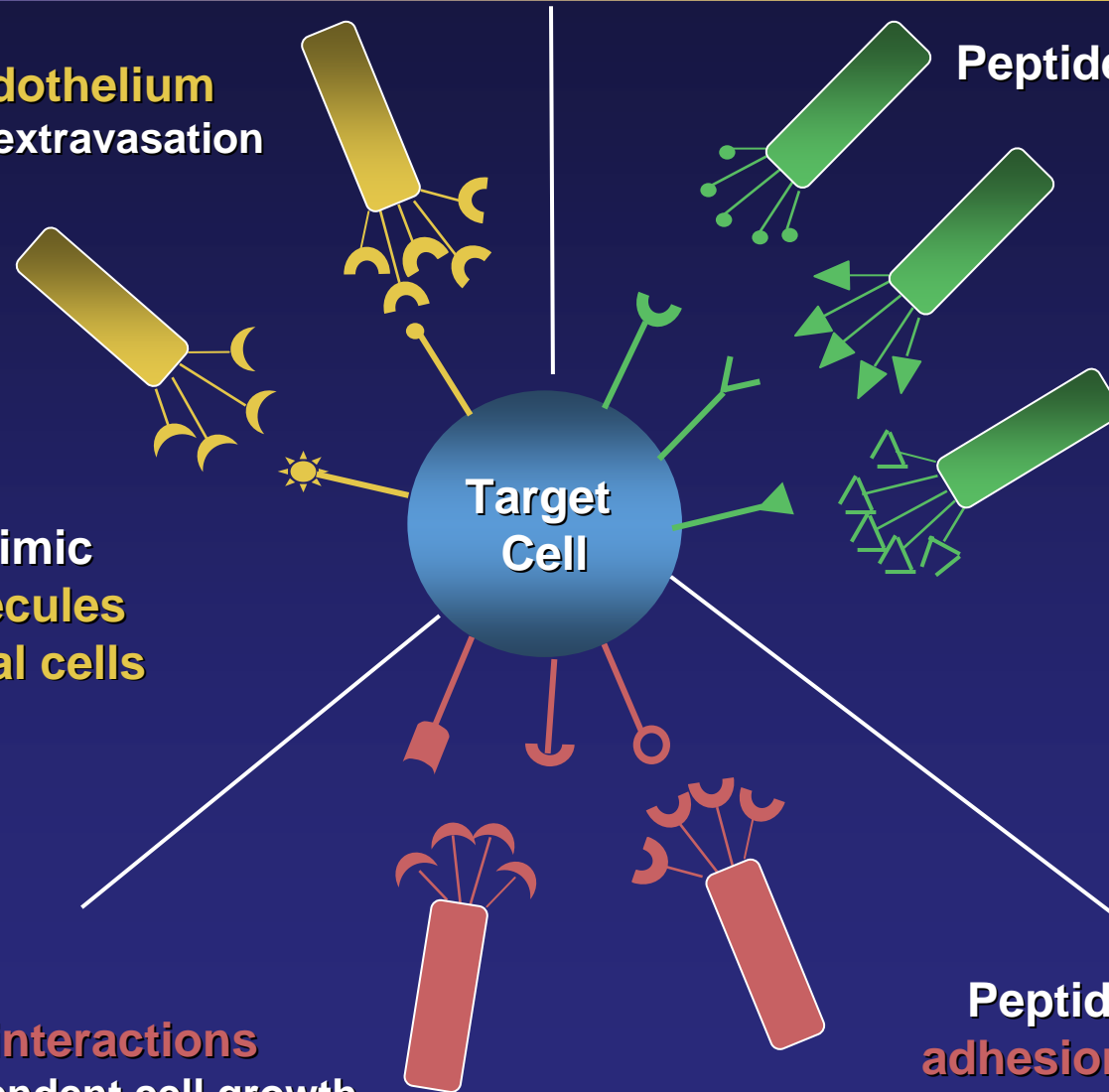
Peptides mimic **ligands**

Peptides mimic  
**surface molecules**  
on endothelial cells

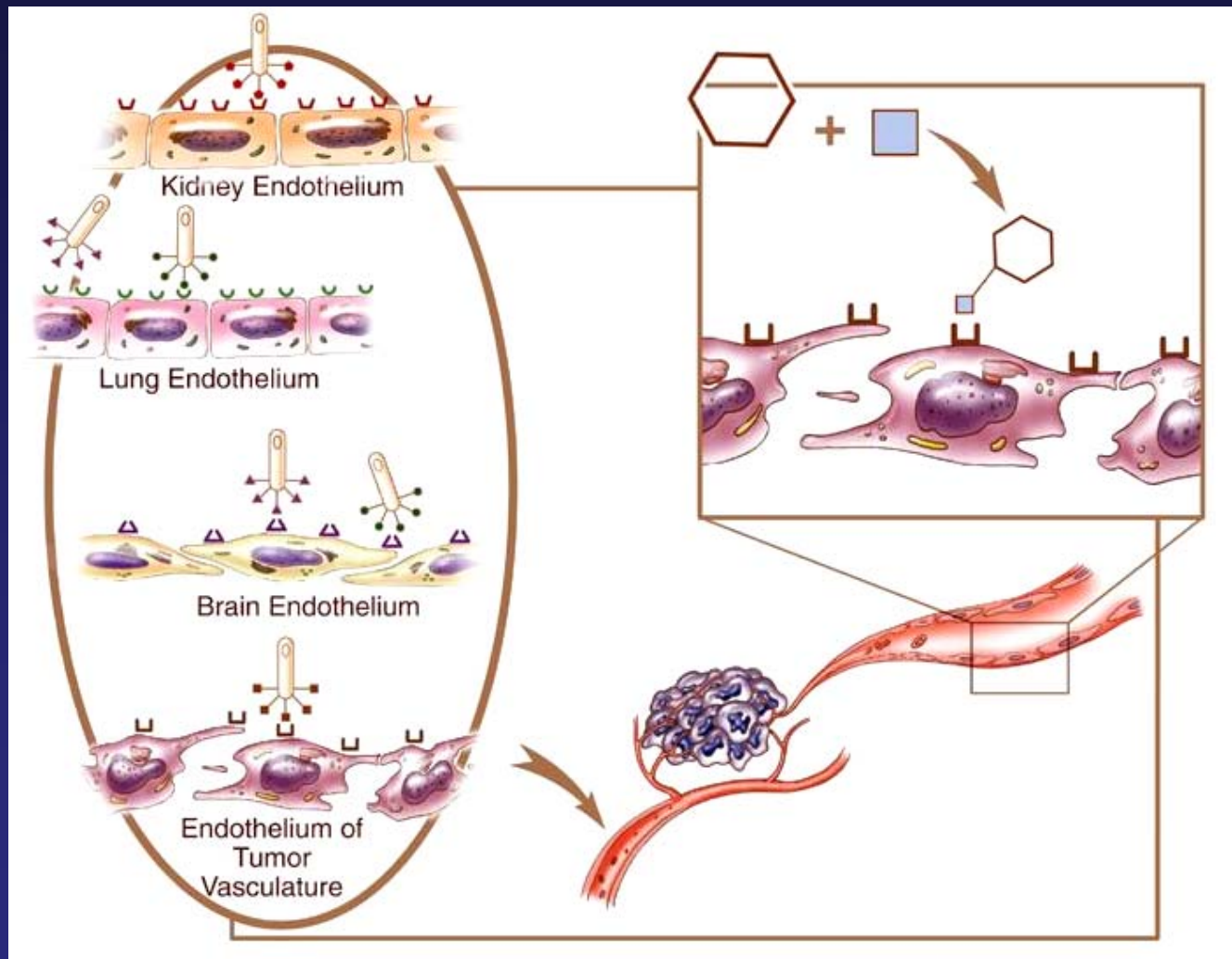
Target  
Cell

Peptides mimic  
**adhesion receptors**  
on tumor cells

**Cell - cell interactions**  
anchorage-dependent cell growth

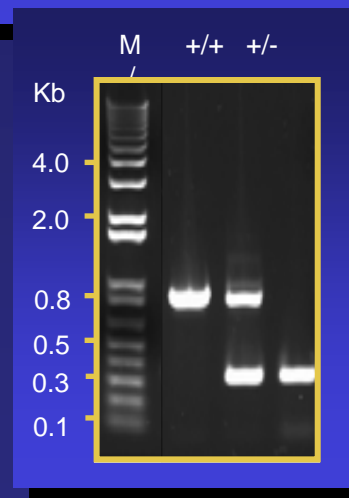
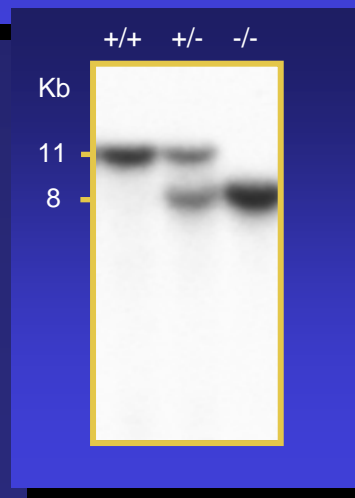
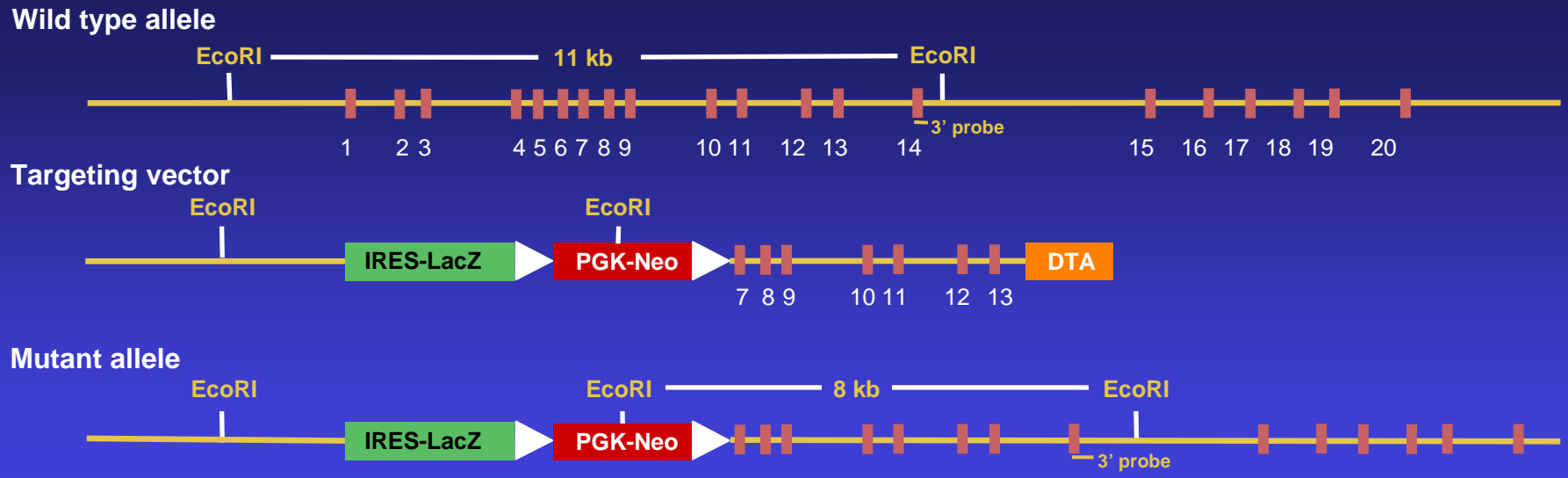


# Organ Vascular Diversity Yields a ZIP Code System



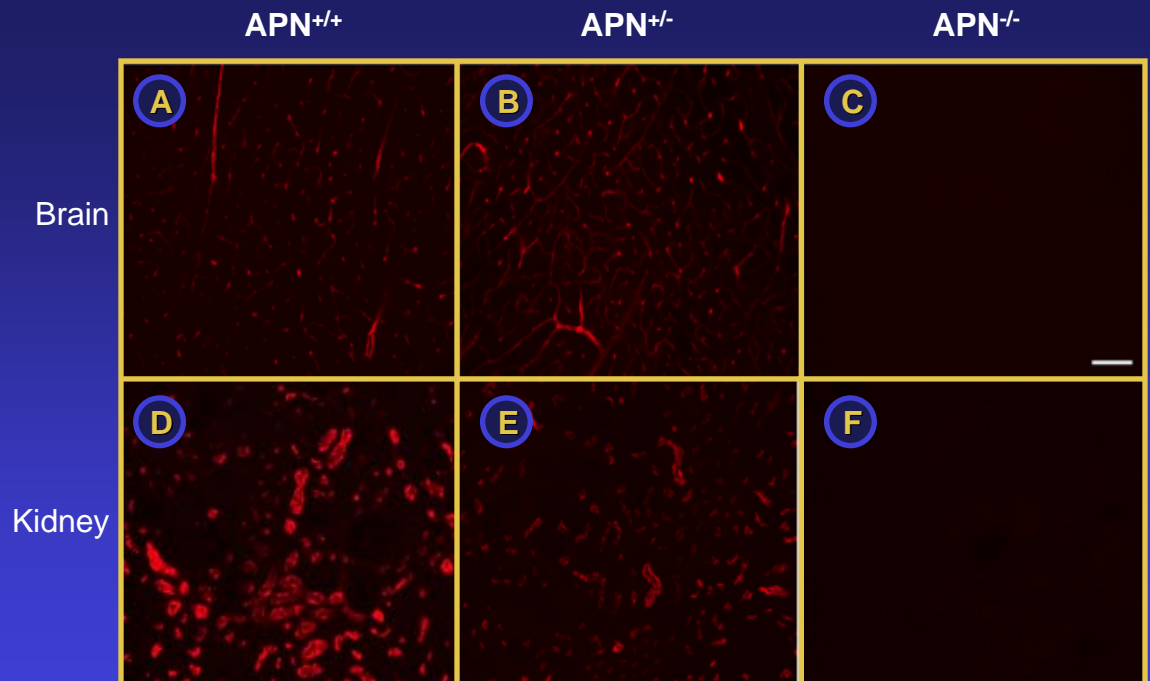
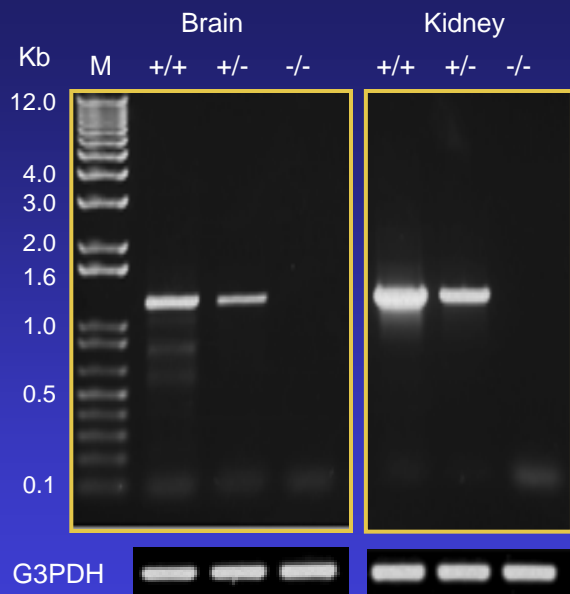
Kolonin et al. *Curr. Opin. Chem. Biol.* 2001

# Design & Construction of the APN-null Mouse

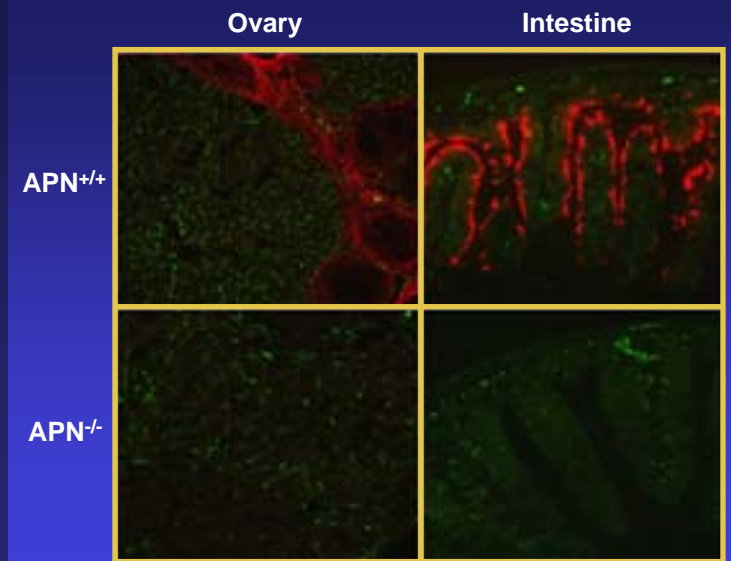
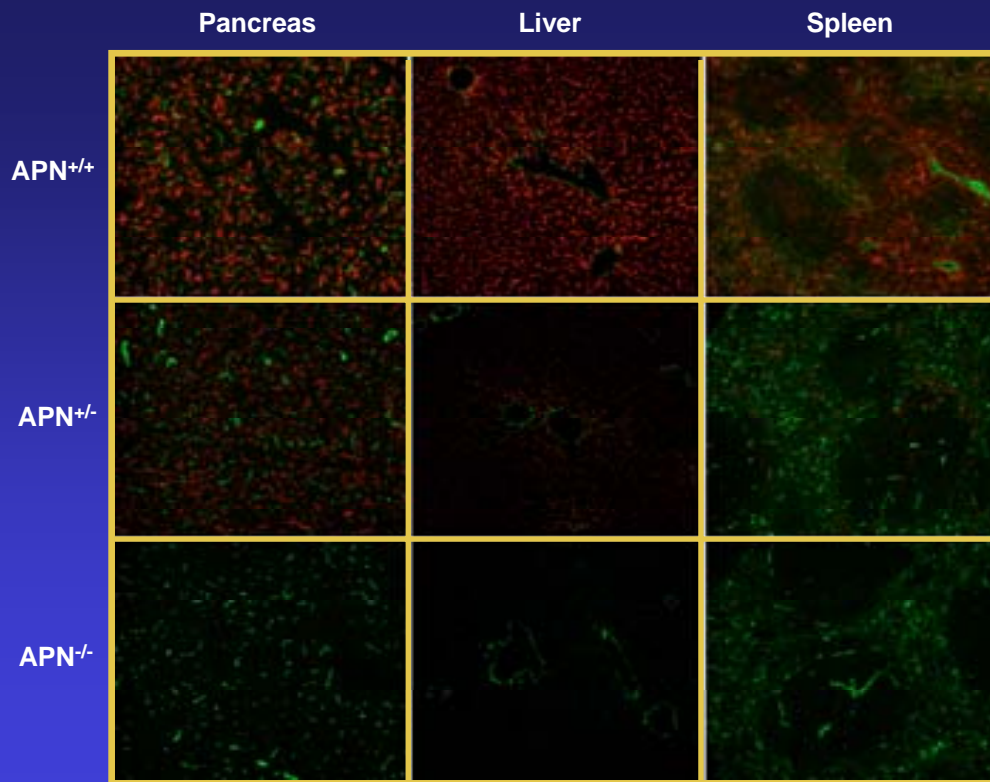


Rangel et al.  
*PNAS* 2007

# Expression Analysis of APN-null Mice



# Immunohistochemical Analysis of APN & CD31

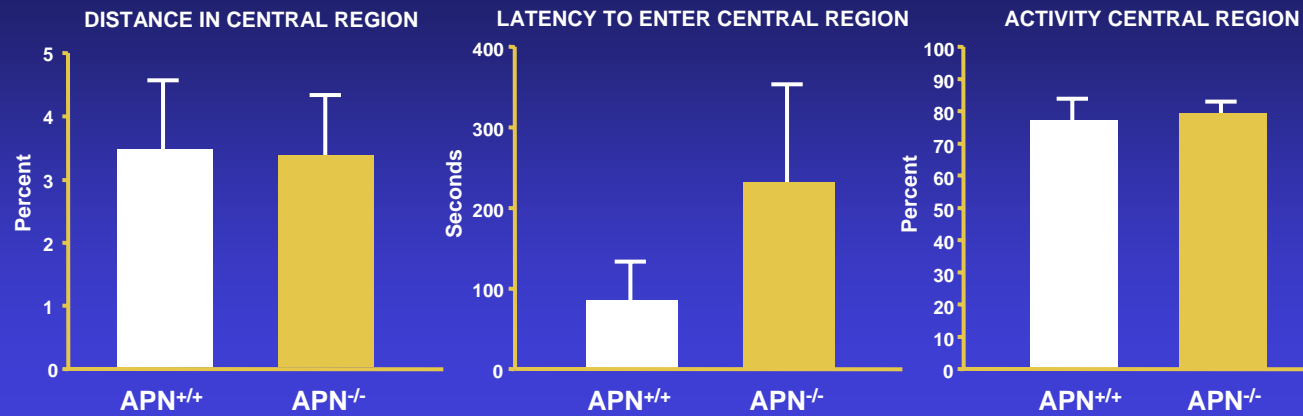


■ CD13    ■ CD31

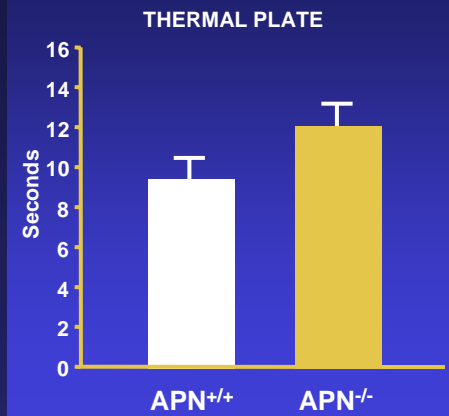
Rangel et al. *PNAS* 2007

# Non-invasive Phenotypic Studies in APN-null Mice

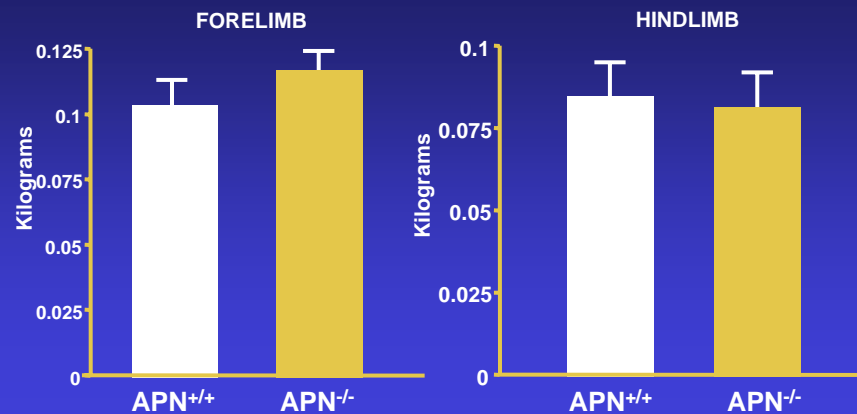
## LOCOMOTOR ACTIVITY



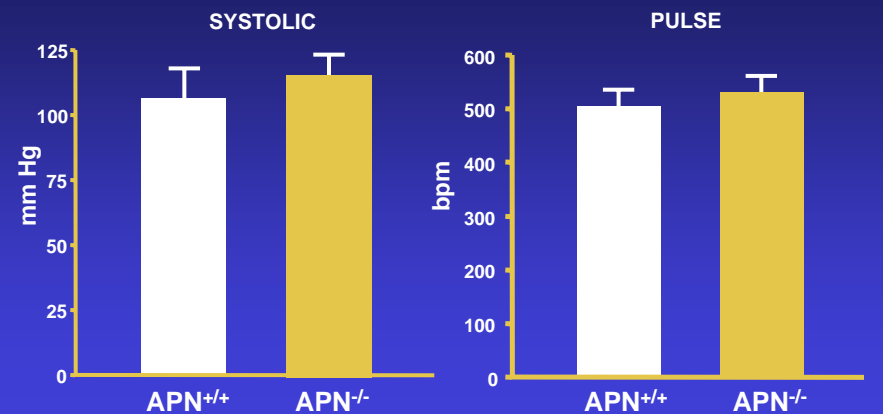
## PAIN REFLEXES



## MUSCLE GRIP STRENGTH

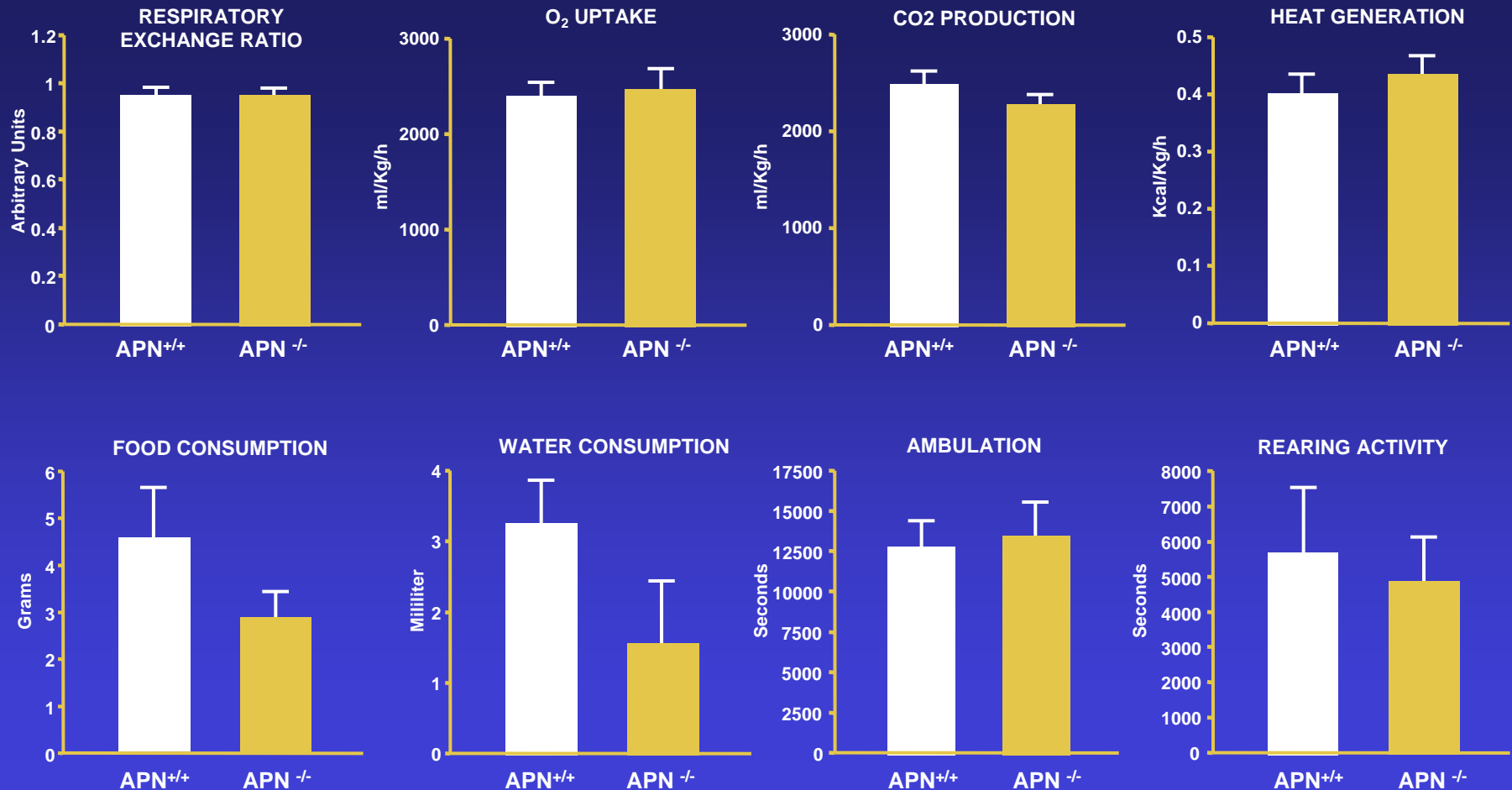


## BLOOD PRESSURE



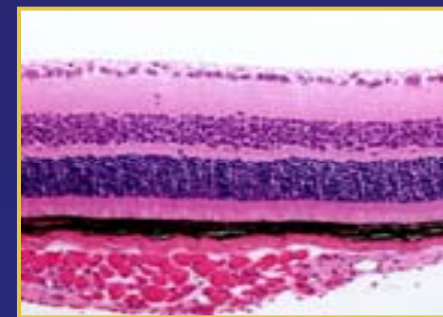
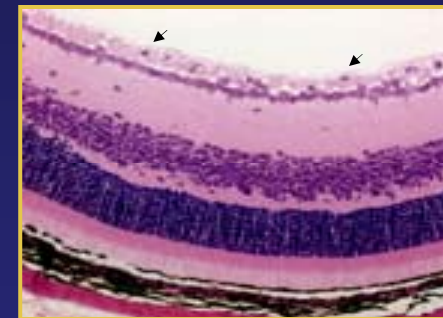
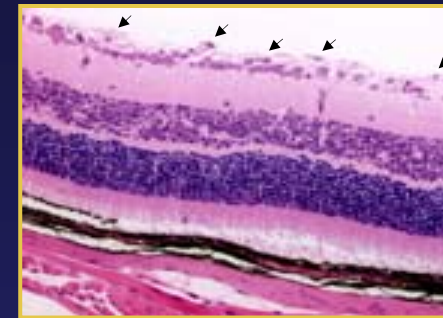
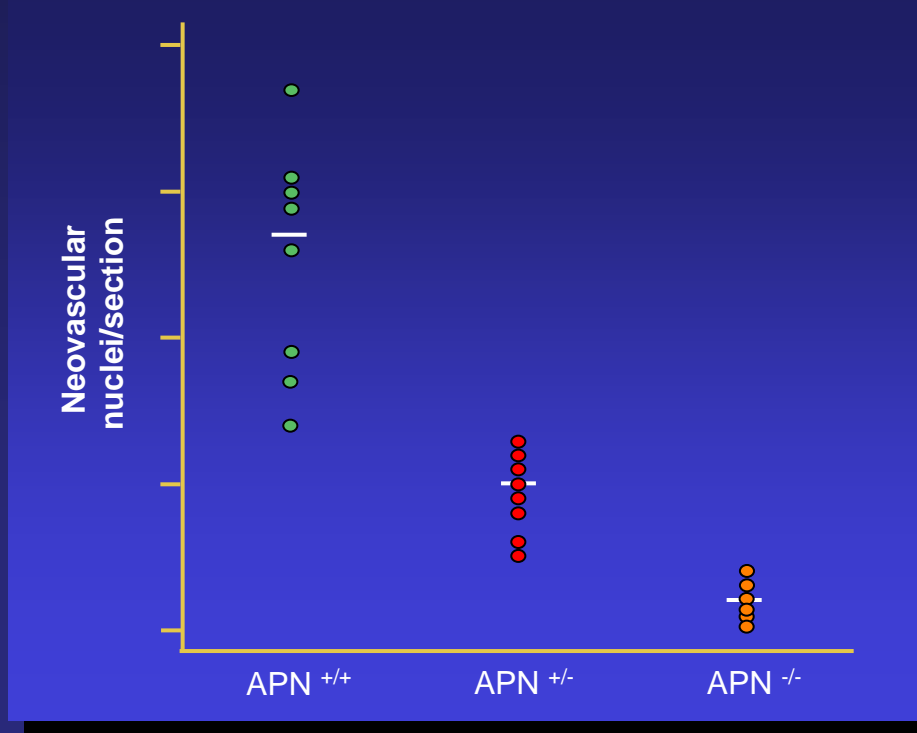
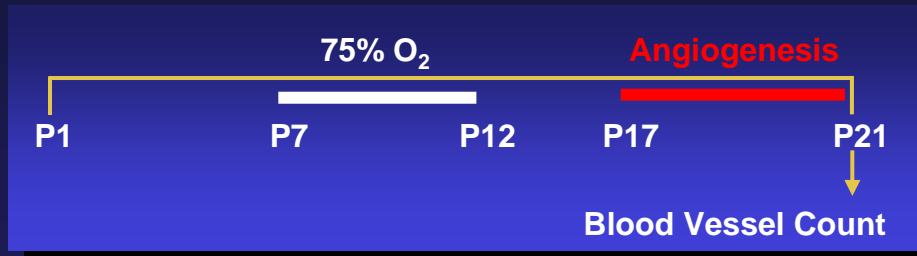
Rangel et al. *PNAS* 2007

# Comprehensive In-cage Monitoring of APN-null Mice



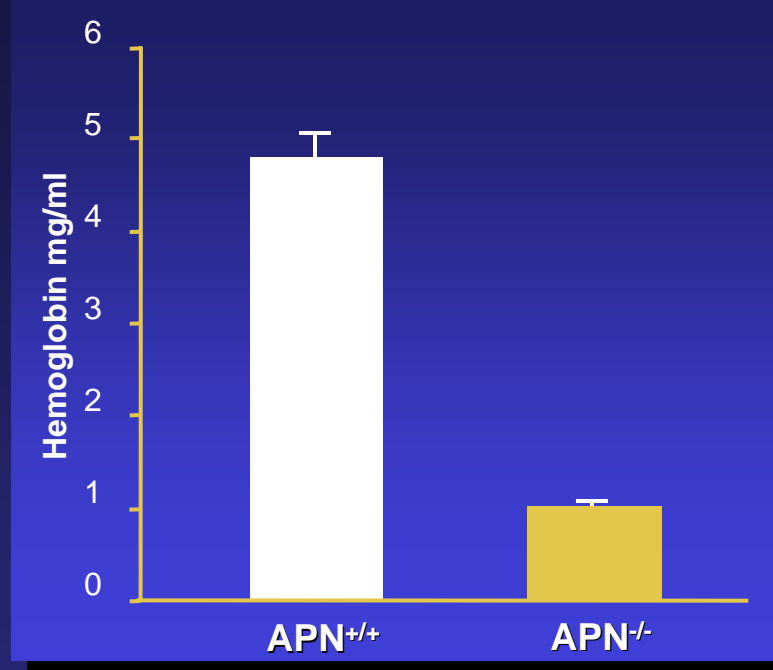


# Failed Retinal Neovascularization in APN-null Mice in Hypoxia



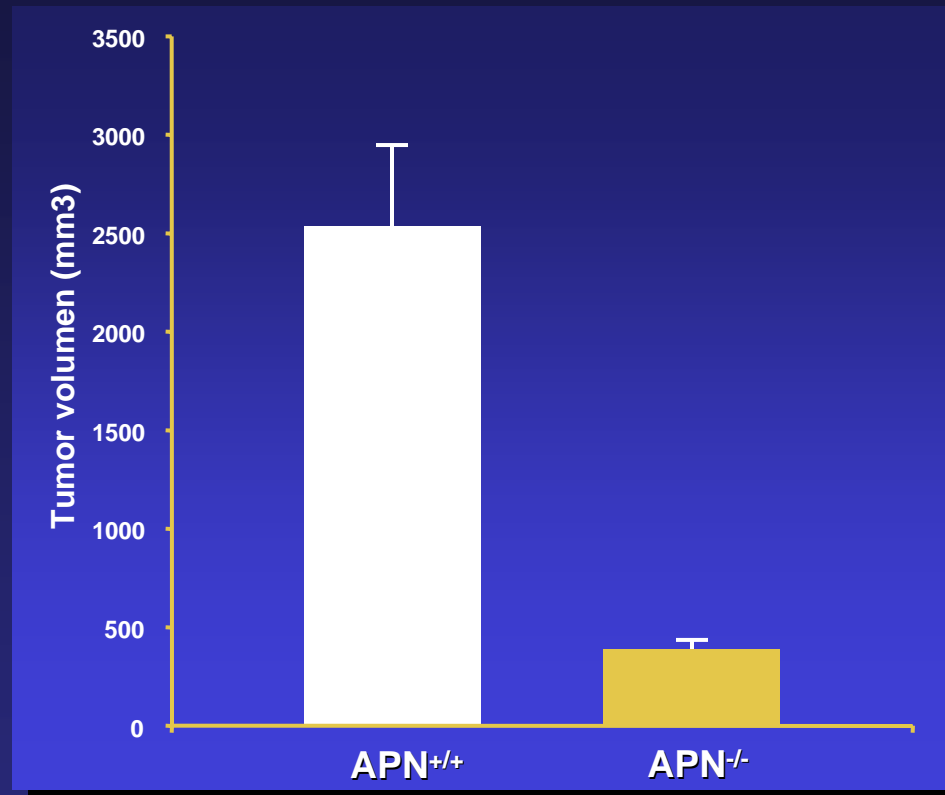
Rangel et al. PNAS 2007

# Impaired Angiogenesis Upon Growth Factor Stimulation in APN-null Mice



Rangel et al.  
*PNAS* 2007

# Growth Inhibition of Tumor Xenografts in APN-null Mice



APN<sup>+/+</sup>



APN<sup>-/-</sup>

Rangel et al.  
(Unpublished)

# Conclusions

- 1. Despite the broad range of CD13 functions, APN-null mice exhibit no developmental, fertility, behavioral or physiological abnormalities.**
- 2. APN-deficient mice display a severely impaired dose-dependent angiogenic response to oxygen-induced retinopathy and angiogenic factors in vivo.**
- 3. APN-null mice may be useful reagents in other medical fields such as malignant, cardiovascular, immunological, or infectious disease.**

# The People

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