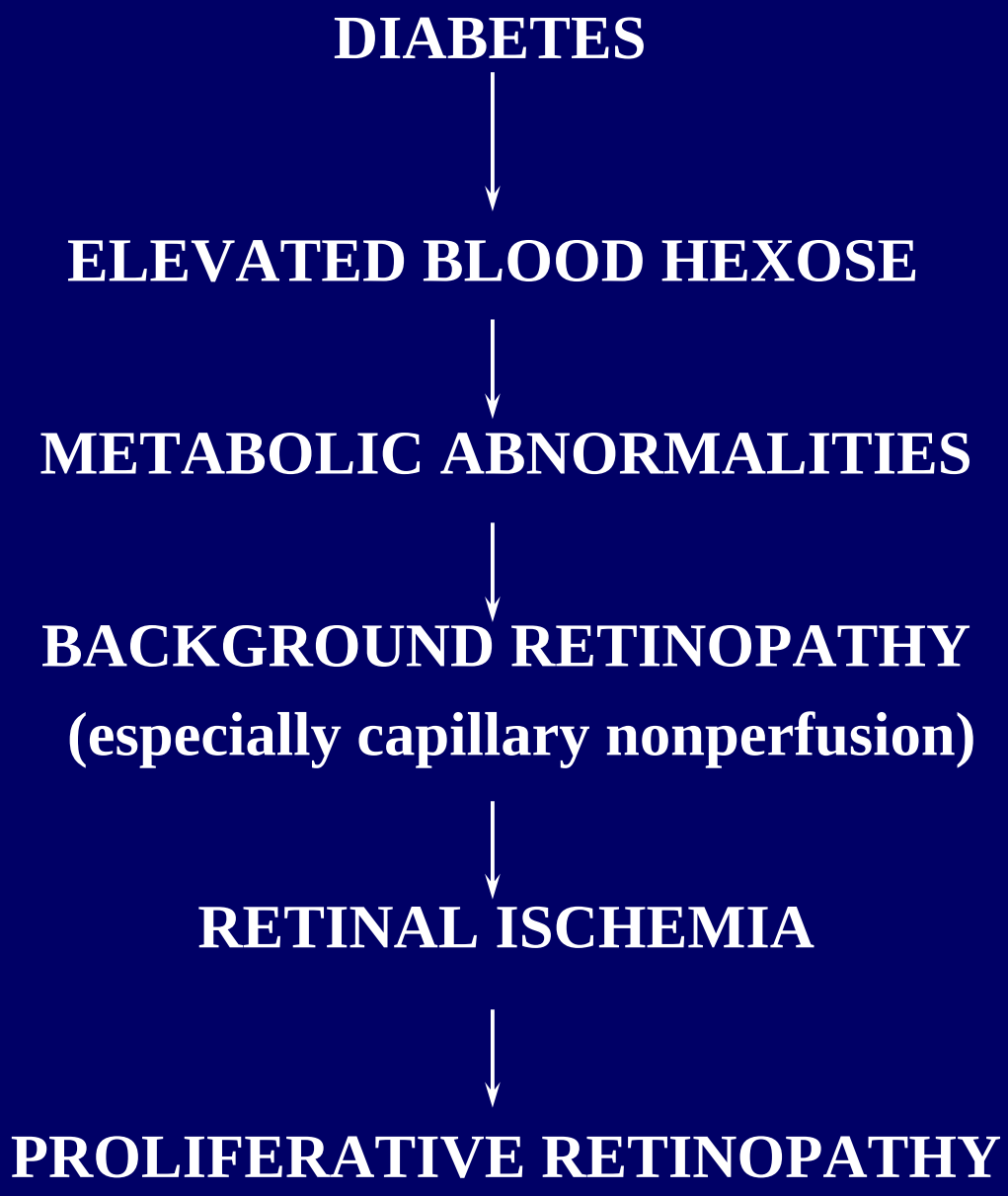
Retinopathy Core

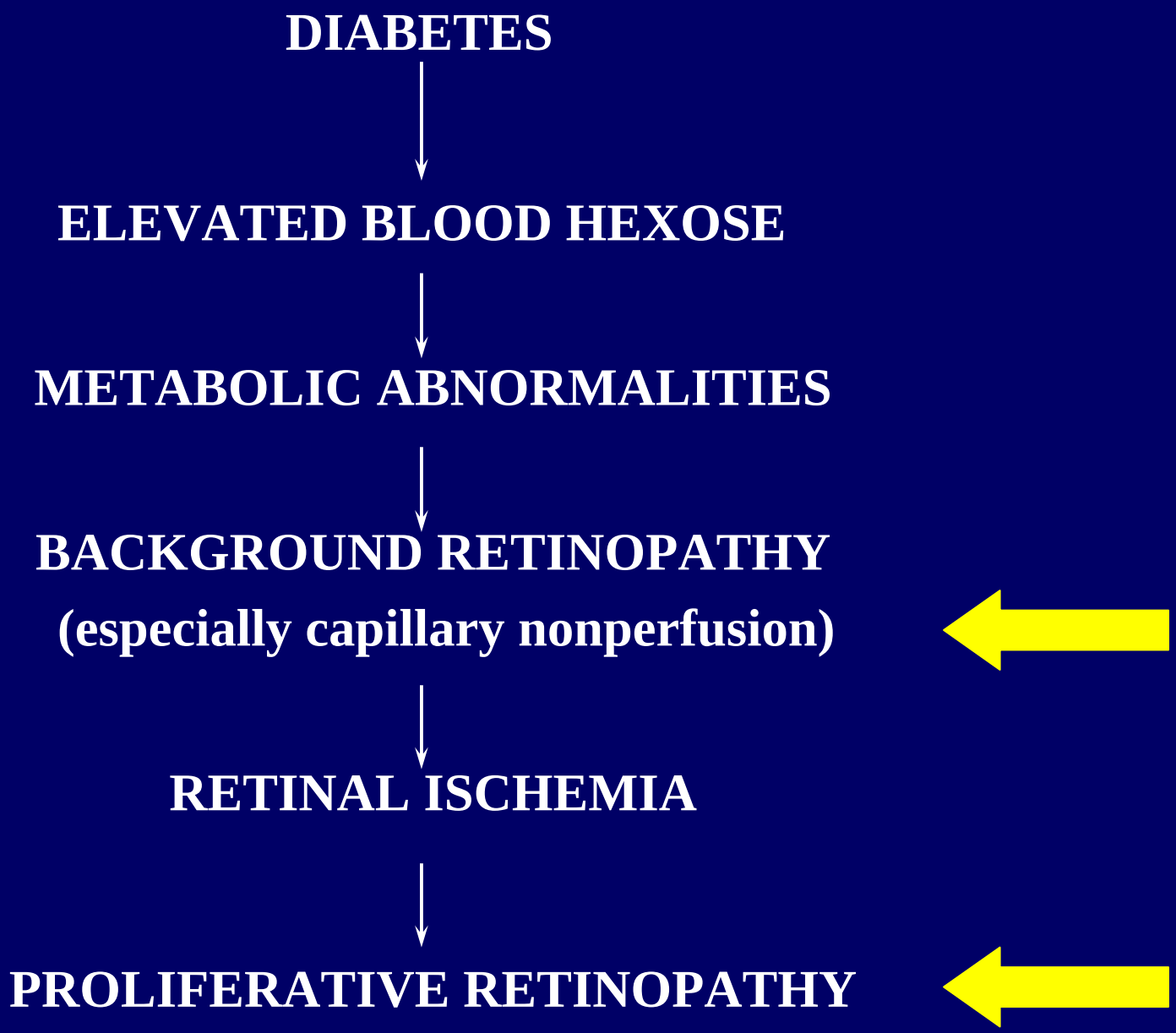
T. Kern, Case Western Reserve Univ

Vascular lesions

- Capillary degeneration
- Neovascularization; not seen

Neurodegeneration


DIABETES
ELEVATED BLOOD HEXOSE
METABOLIC ABNORMALITIES
BACKGROUND RETINOPATHY
(especially capillary nonperfusion)
RETINAL ISCHEMIA
PROLIFERATIVE RETINOPATHY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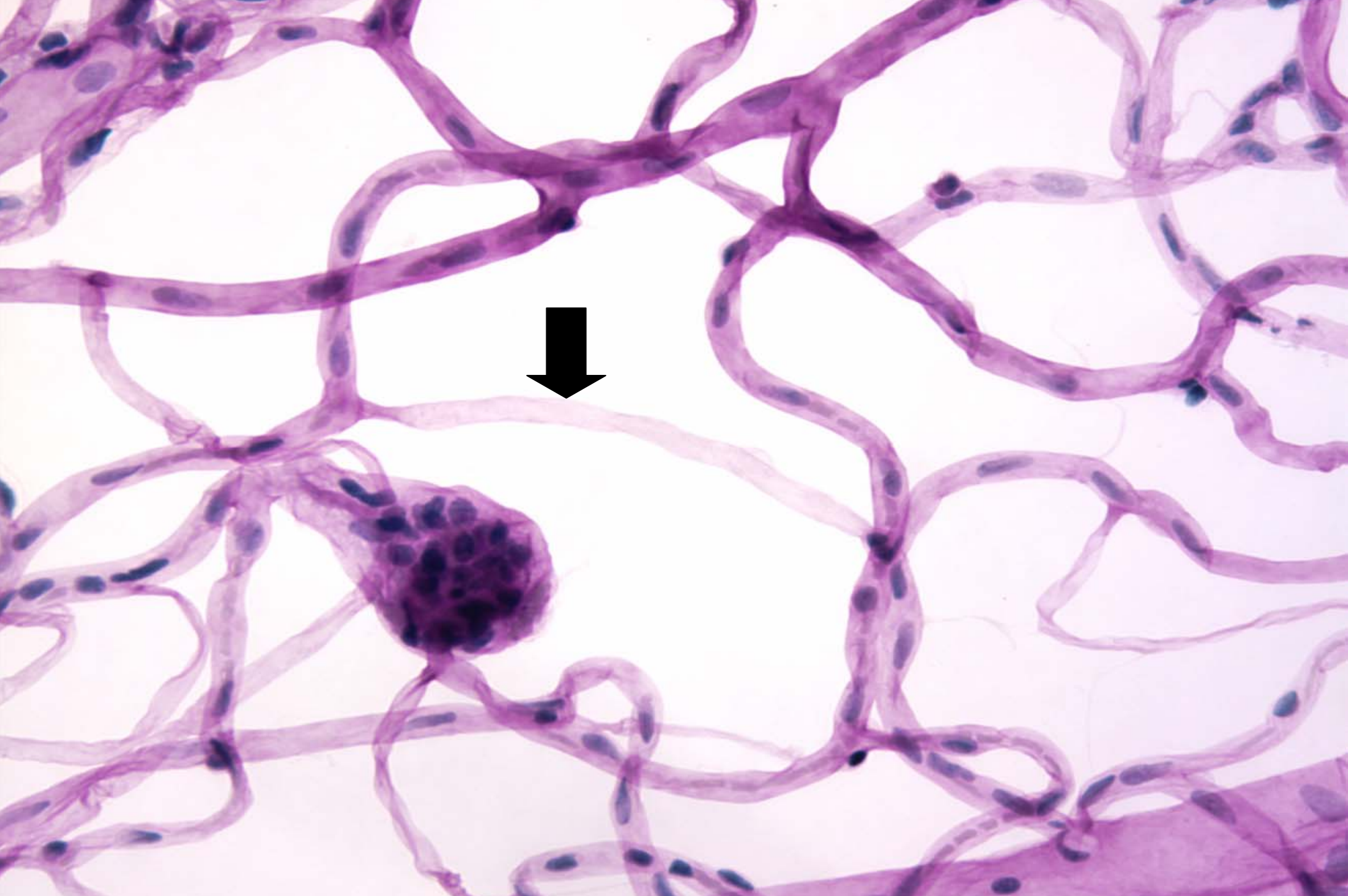
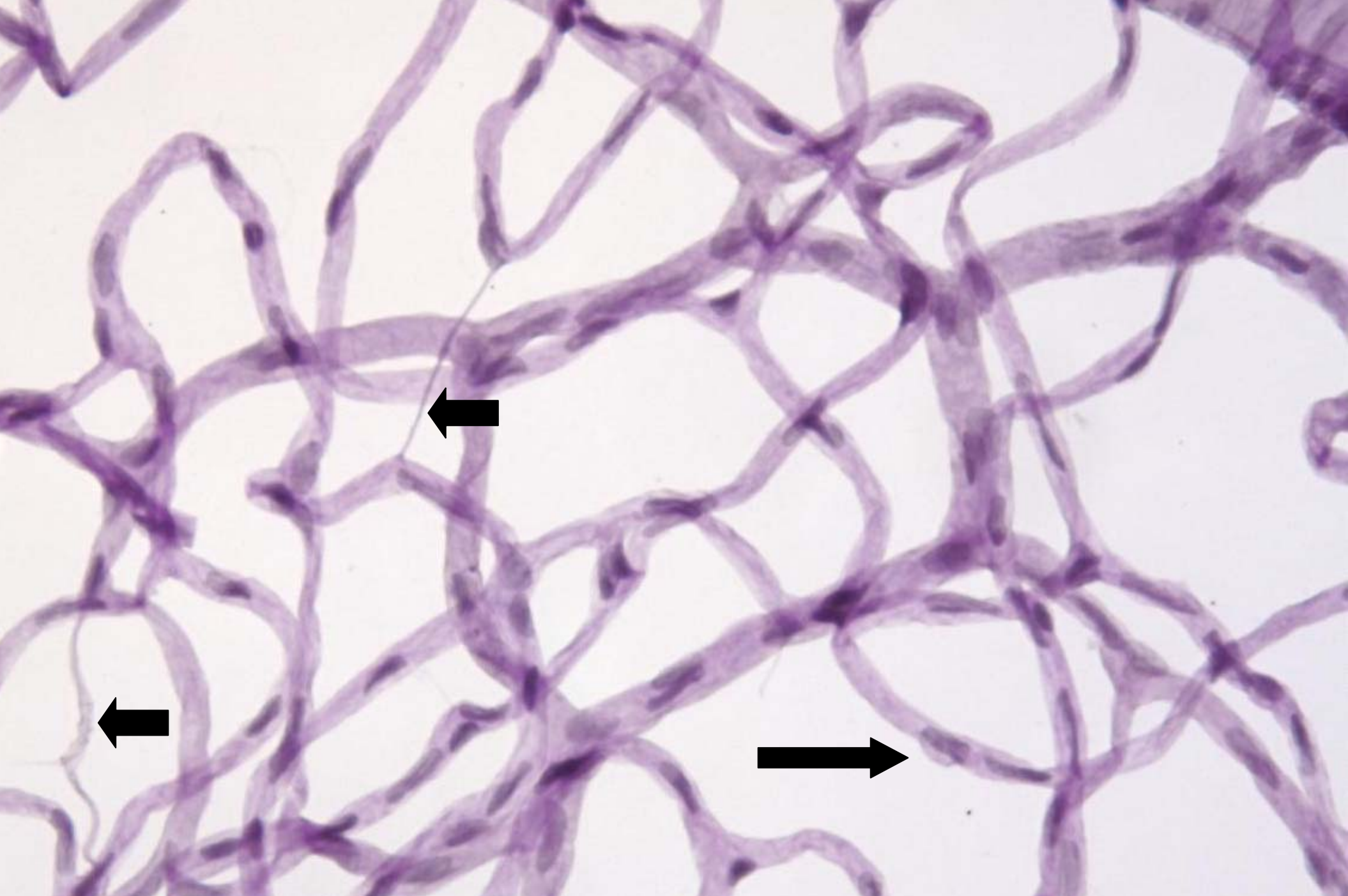
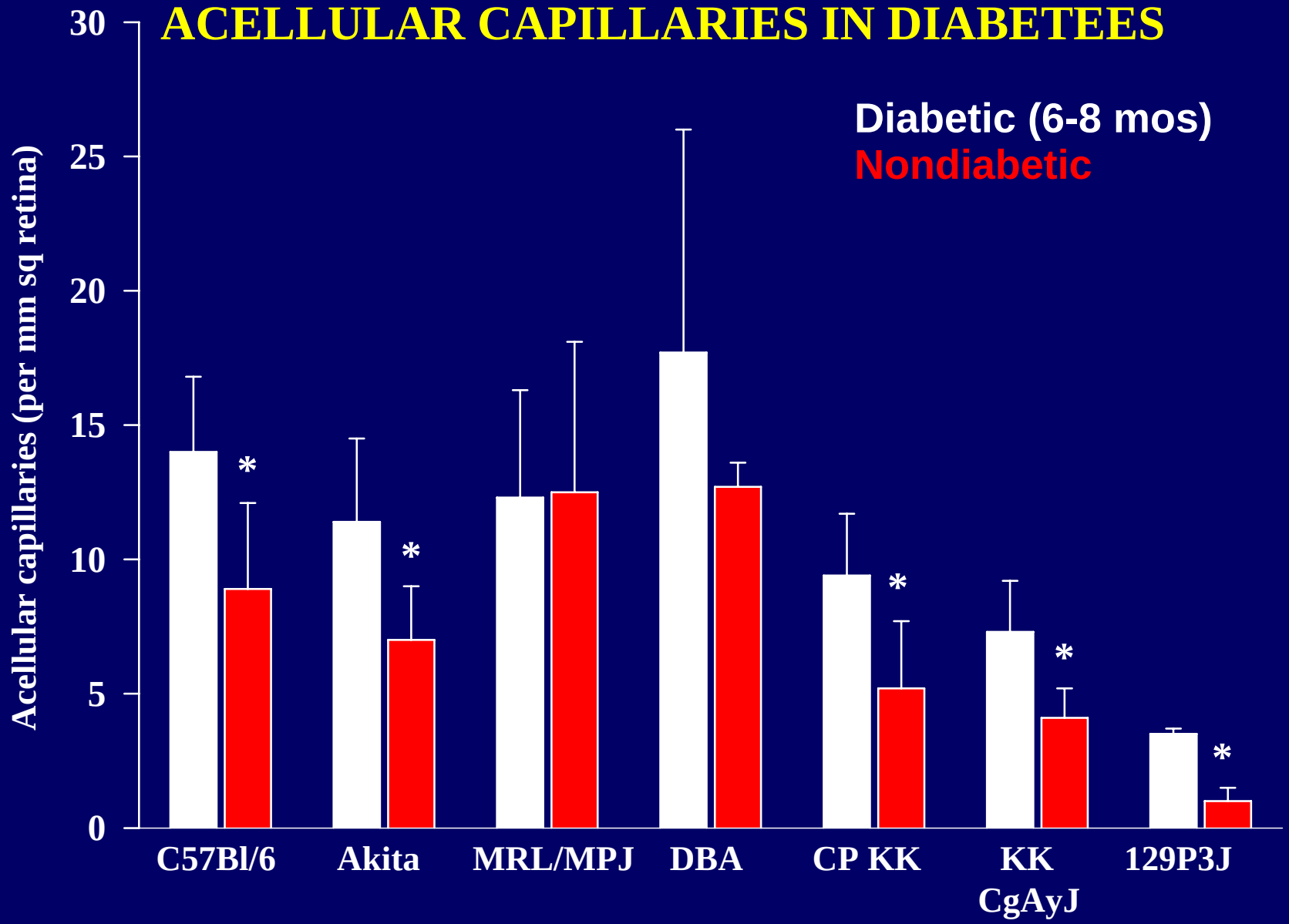




STRAIN DIFFERENCES IN DEVELOPMENT OF RETINAL ACELLULAR CAPILLARIES IN DIABETEES

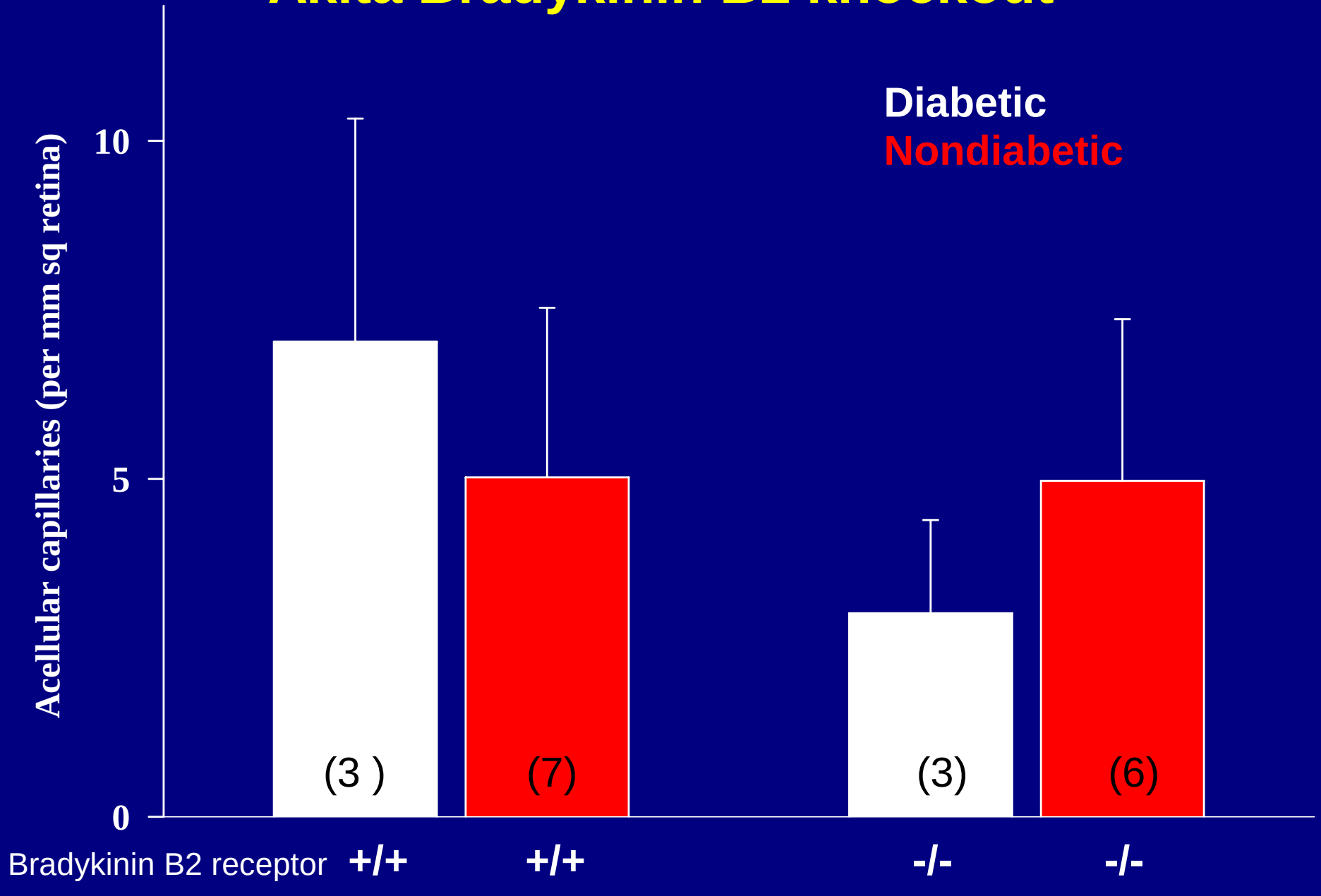


* P<0.05 compared to untreated control

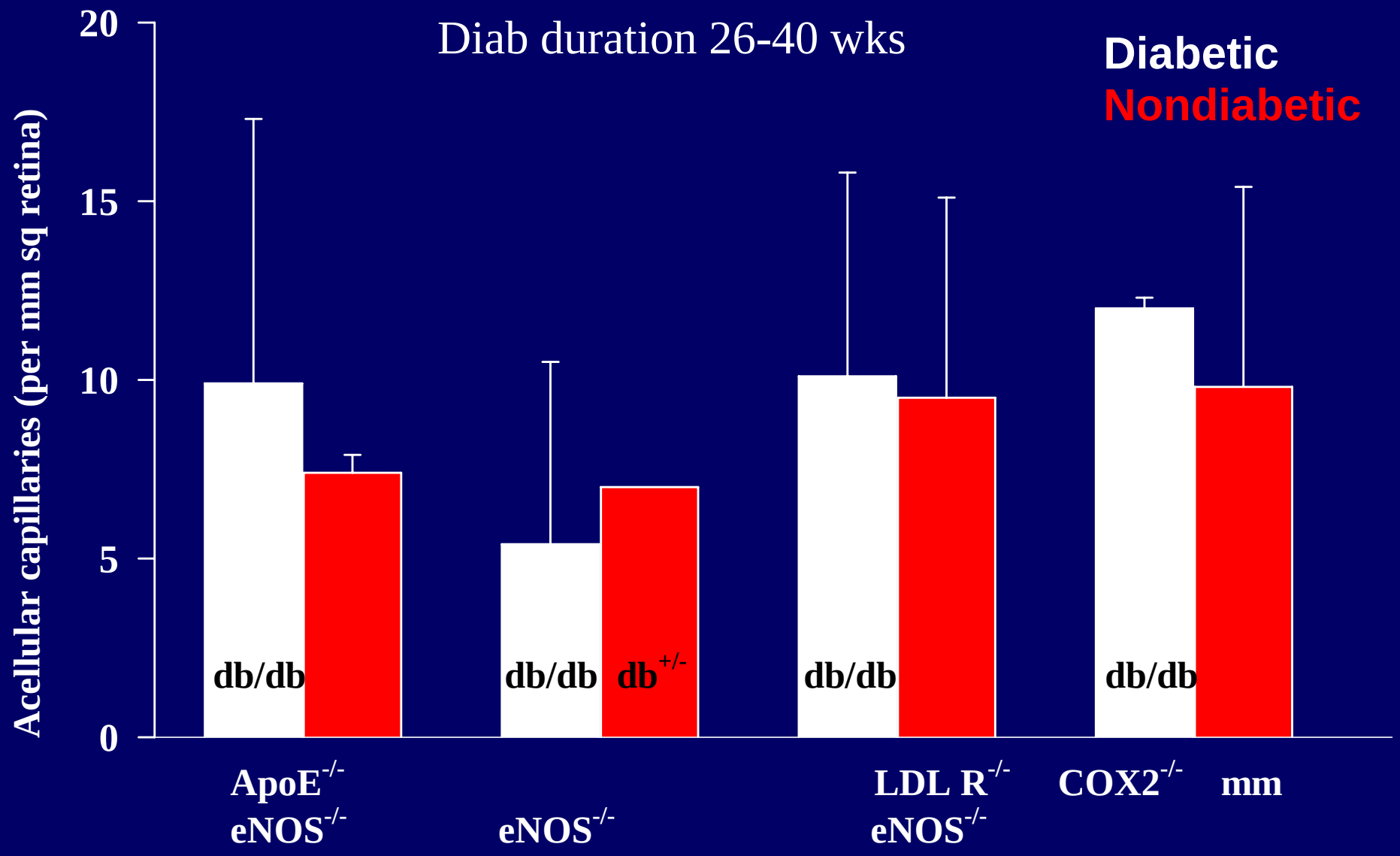
Mice

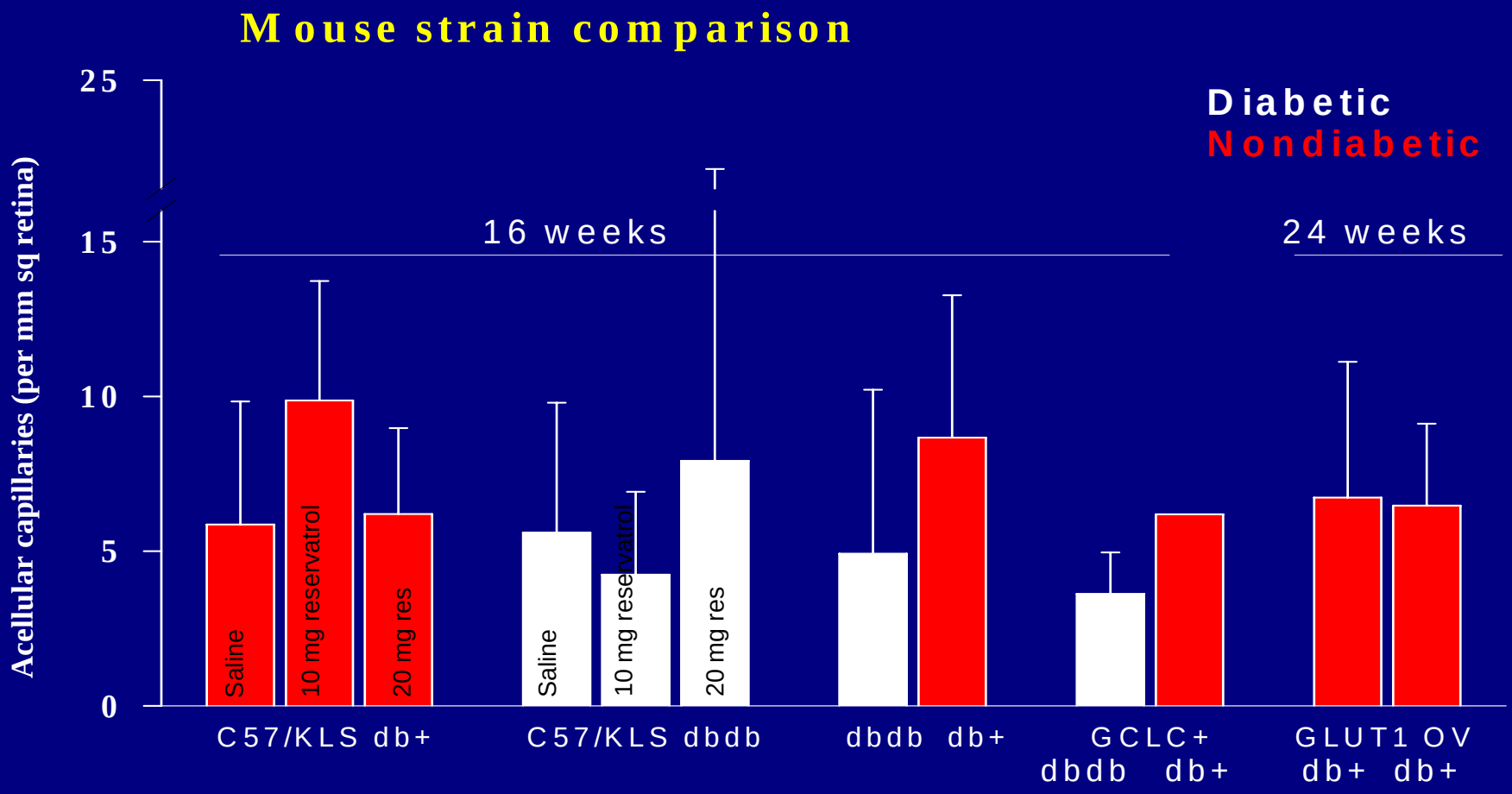
• Akita Bradykinin B2 R-/-	Coffman
• Akita	Kern
• C57 Pdx x LDL-/-	Feldman
• DBA/2	Inman
• GCLC dbdb with and without high fat diet	Feldman
• Glut 1 Overexpressors x dbdb on high fat	Feldman
• KLSdbdb with 3 concentrations of resvervatrol	Feldman
• LDLR-/- x eNOS-/- dbdb	Harris
• ApoE-/-	Harris
• COX2-/-	Harris

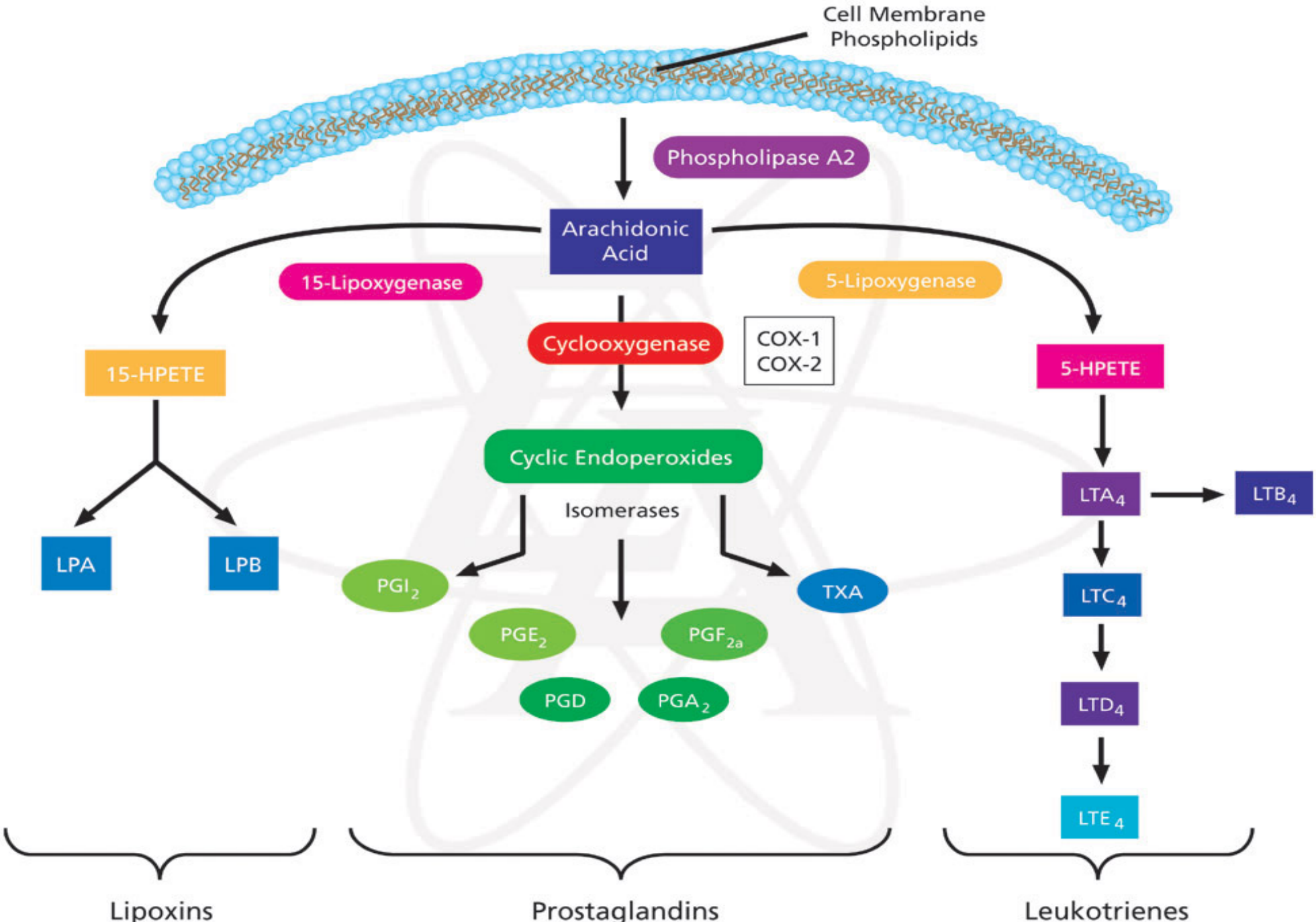
Akita Bradykinin B2 knockout



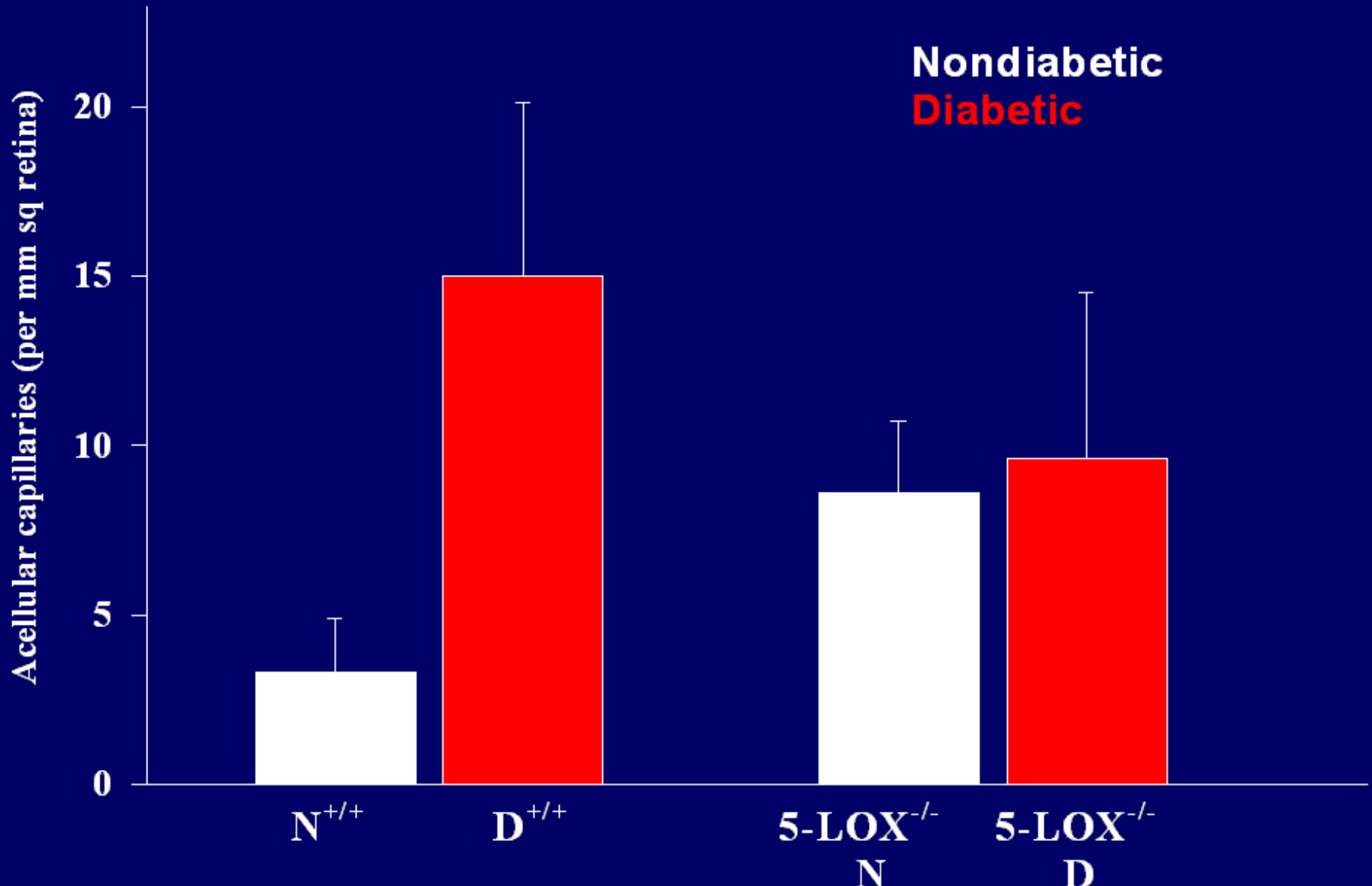
Mouse models of diabetic retinopathy




Mouse strain comparison
Diabetic
Nondiabetic
Acellular capillaries (per mm sq retina)
25
15
10
5
0
16 weeks
24 weeks
Saline
10 mg reservatrol
20 mg res
Saline
10 mg reservatrol
20 mg res
C57/KLS db+
C57/KLS dbdb
dbdb db+
GCLC+ dbdb db+
GLUT1 OV db+ db+


Cell Membrane Phospholipids
Phospholipase A2
Arachidonic Acid
15-Lipoxygenase
5-Lipoxygenase
Cyclooxygenase
COX-1
COX-2
15-HPETE
5-HPETE
Cyclic Endoperoxides
Isomerases
LPA
LPB
PGI2
TXA
PGE2
PGF2a
PGD
PGA2
LTA4
LTB4
LTC4
LTD4
LTE4
Lipoxins
Prostaglandins
Leukotrienes

DELETION OF 5-LIPOXYGENASE SLOWS DEVELOPMENT OF RETINAL ACELLULAR CAPILLARIES IN DIABETES



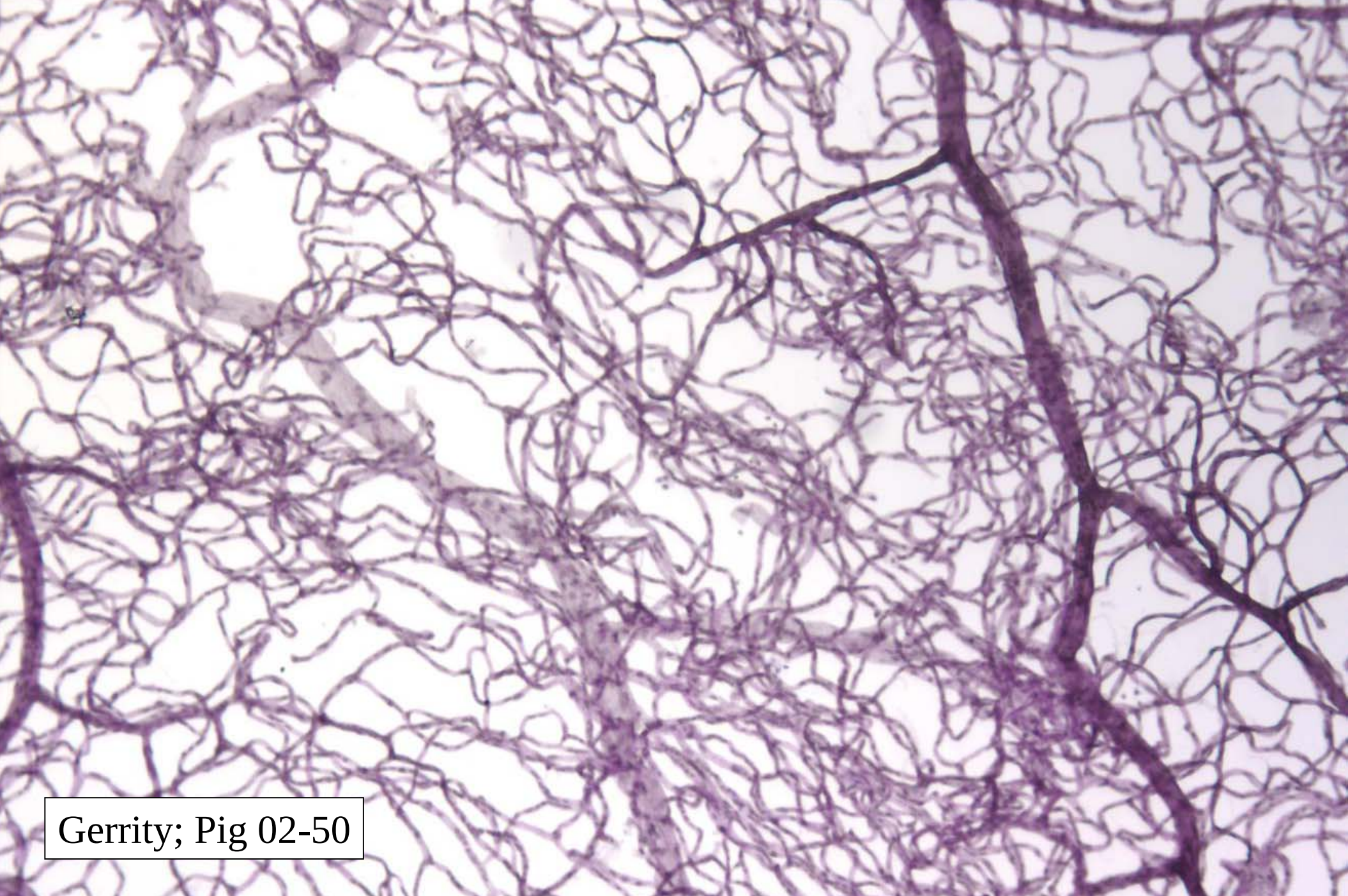
Pig models

- **high fat diet/high carbohydrate**

  Type 2 diabetes (insulin resistant)

- **high fat diet + STZ diabetes**

  Type 1 diabetes


Gerrity; Pig 02-50

Thanks to:

NIH
JDRF
EAC
AMDCC MEMBERS

KEEP SENDING SAMPLES