The Amyloid Plaque Microenvironment

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INTRODUCTION

• Amyloid plaques are a key feature of AD
• Most of what we know about amyloid biology is based on mouse models

*How does the plaque microenvironment differ between mice and humans?*

METHODS

Evaluate tissue from APP/PS1 mice, aged rhesus monkeys, and humans with AD

• Immunofluorescence
  • Glial fibrillary acidic protein (GFAP)
  • Voltage dependent anion channel (VDAC)
• Histochemistry
  • Cytochrome c oxidase activity
• Multiphoton Laser Scanning Microscopy (MPLSM)
  • NAD(P)H
• Amyloid plaques co-localize with high mitochondrial density
• The location of these mitochondria differs between species

• Mitochondria in the plaque vicinity have high complex IV activity
• Amyloid plaques have a unique fluorescence signature detectable by MPLSM/FLIM
SUMMARY

• Amyloid plaques co-localize with activated astrocytes and functionally distinct mitochondria
• There are important differences in the amyloid microenvironment between primates and rodents
• Plaques have a unique metabolic signature detectable by MPLSM/FLIM

QUESTIONS

• What is the impact of age on the tissue response to amyloid?
• How does the age of the plaque itself affect the tissue response?