

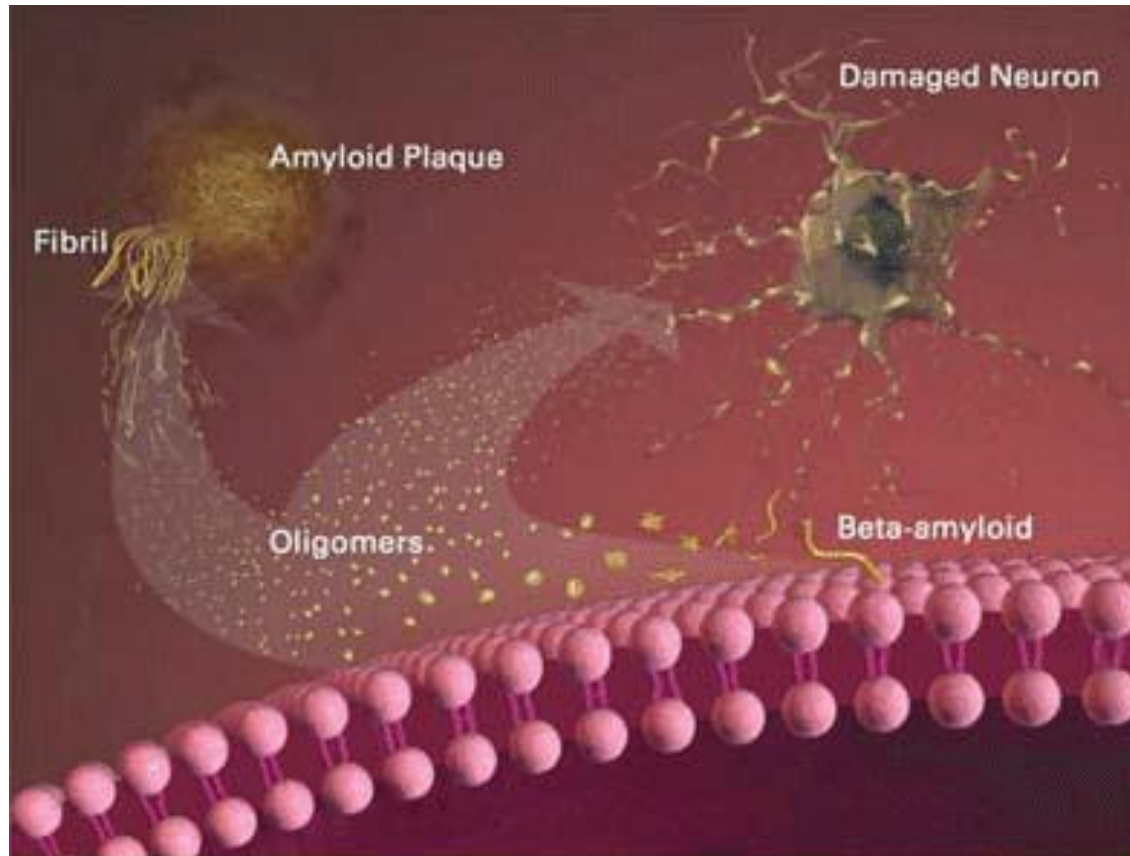
Diagnostic A β O- targeted probes for Alzheimer's Disease

Nafay Abdul and Sophia Pribus

Alzheimer's Disease

- 1 person develops AD every 65 seconds
- treatment cost US \$277 billion in 2018
- plaques and tangles develop between nerves and inside cells
- symptoms: memory loss, confusion, difficulty speaking, swallowing and walking

A β oligomers vs Fibrillar Amyloids



A β O Hypothesis

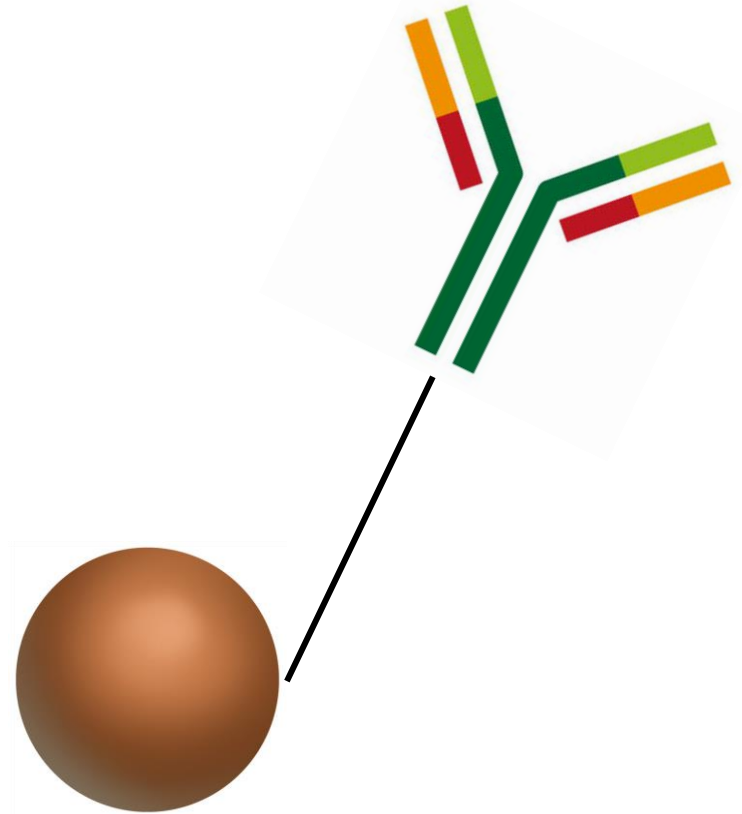
The accumulation and deposition of oligomeric or fibrillar amyloid β (A β) peptide is the primary cause of Alzheimer's disease (AD)

Current AD Diagnostics

- **MRI** → used to quantify brain volume/measure brain metabolism
- **Probes** → used to target certain structures for imaging
 - e.g. PET probes → quantify ThioS-positive amyloid plaques
- No probe specifically for A β O_s

A β O Probe

- Attach oligomer-specific antibodies onto magnetic nanostructures
- Binds to A β oligomers to give a magnetic resonance imaging signal



Methodology

- Protein assays
 - testing and improving conjugation efficiency of MNS to antibodies
 - optimal method - double treatment
- In vivo testing
 - mouse model
 - rabbit model
- Immunohistology
 - Sliced Brain Cells
 - Immunofluorescent

Probe Development Data

Original Probe

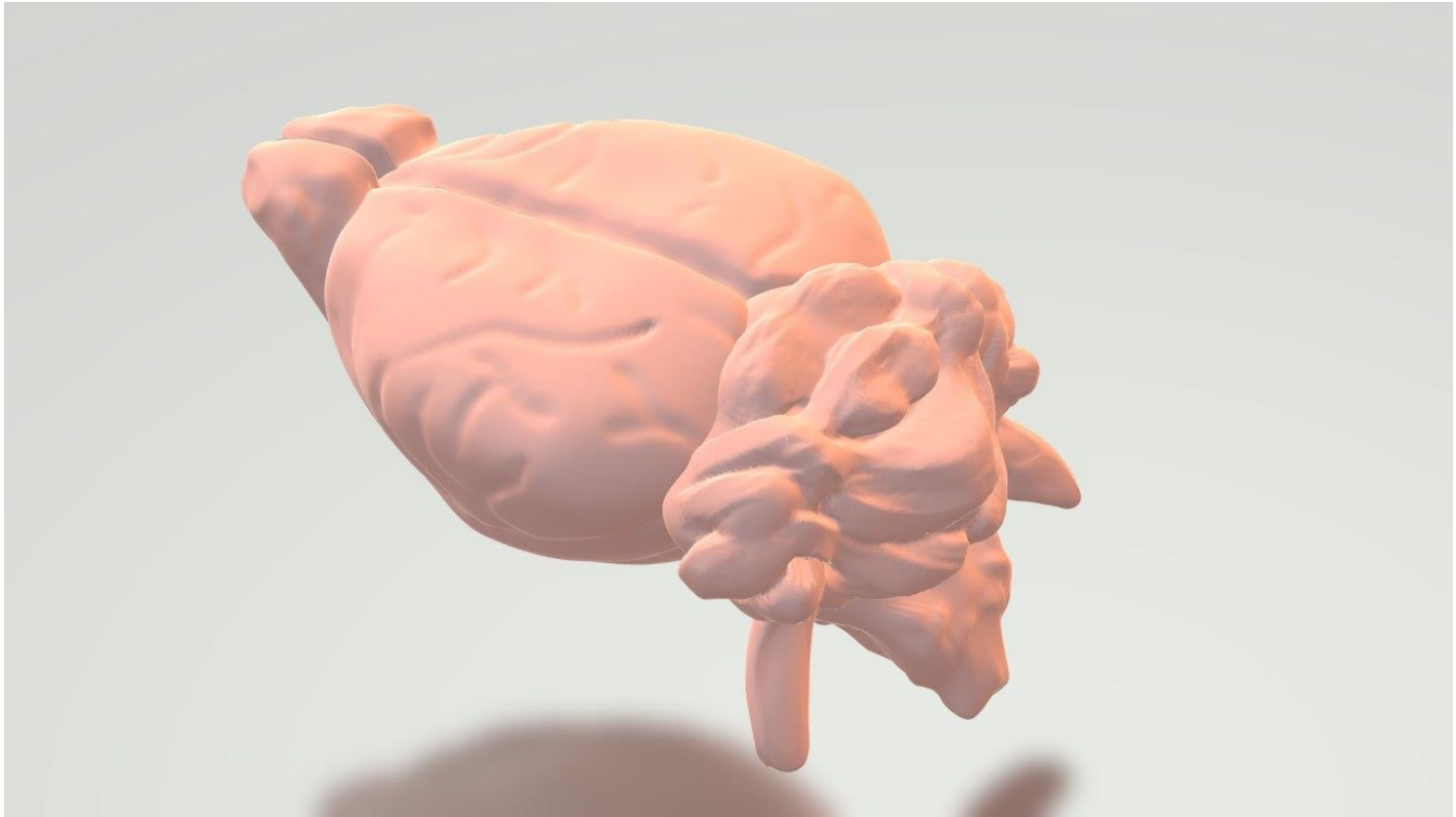
	Antibody 1	IgG antibody 1	Antibody 3	Antibody 4	IgG antibody 2	IgG antibody 3
Average	.2545	.226	.219	.2435	.223	.222
Protein Concentration	.179	.139	.129	.163	.135	.133
Percent Conjugation	35.74%	27.76%	25.80%	32.66%	26.92%	26.64%

Modified Probe

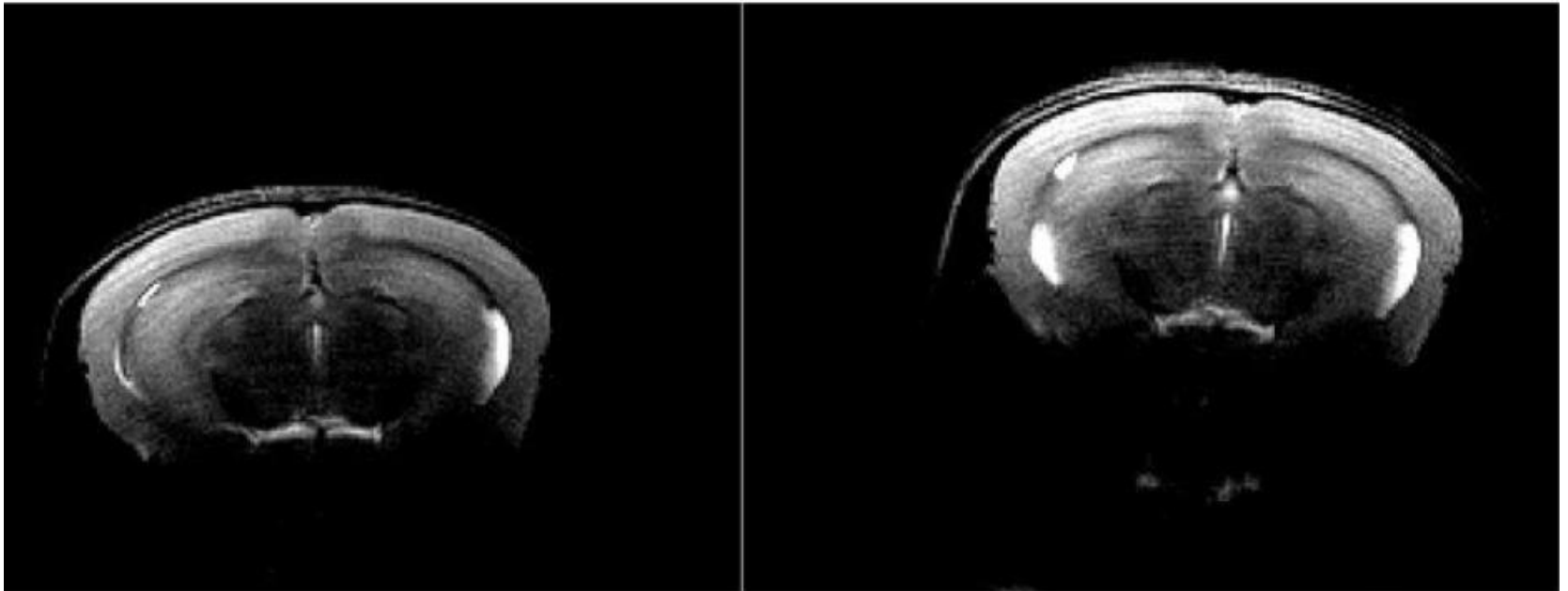
	Antibody 1	Antibody 2	Antibody 3	Antibody 4	Antibody 5	Antibody 6	Antibody 7
Average	.579	.7415	1.08	1.33	.1.51	1.79	2.08
Protein Concentration	7.02	9.08	13.38	16.51	18.88	22.33	26.13
Percent Conjugation	73%	73%	73%	73%	73%	73%	73%

Mice Data

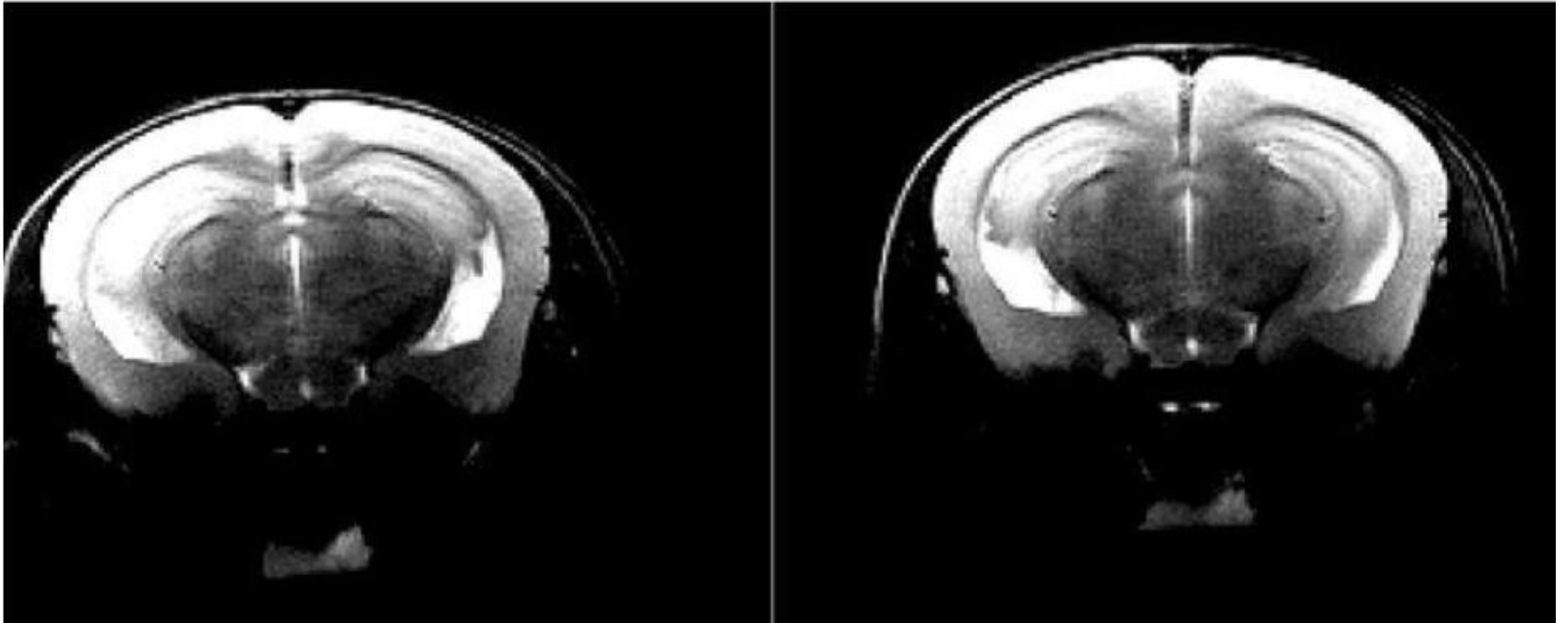
Mouse Brain Model



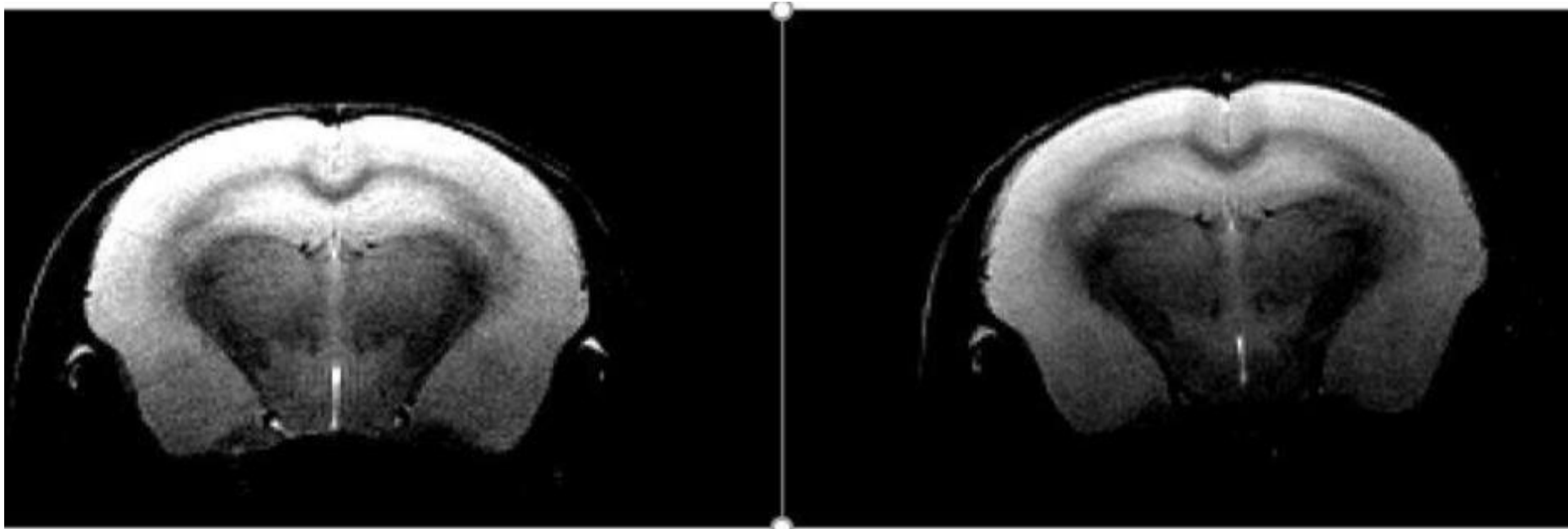
Probe In Mouse



Probe In Mouse

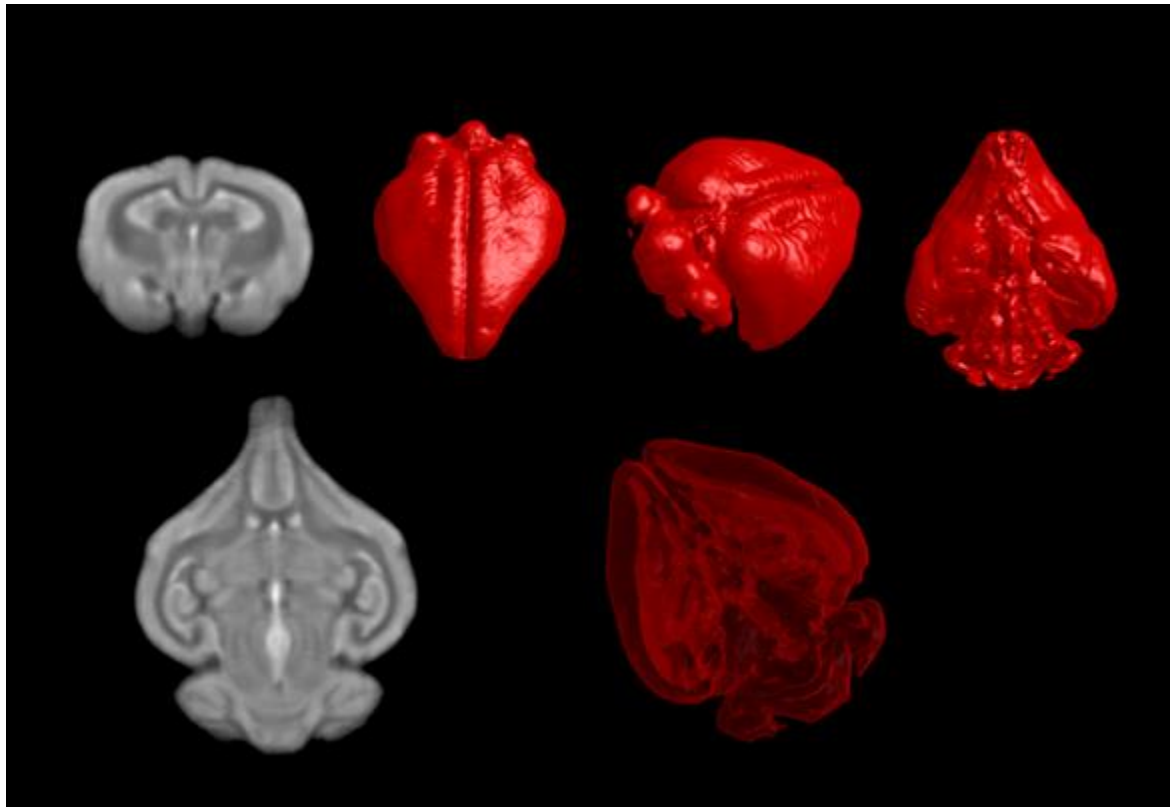


Probe In Mouse

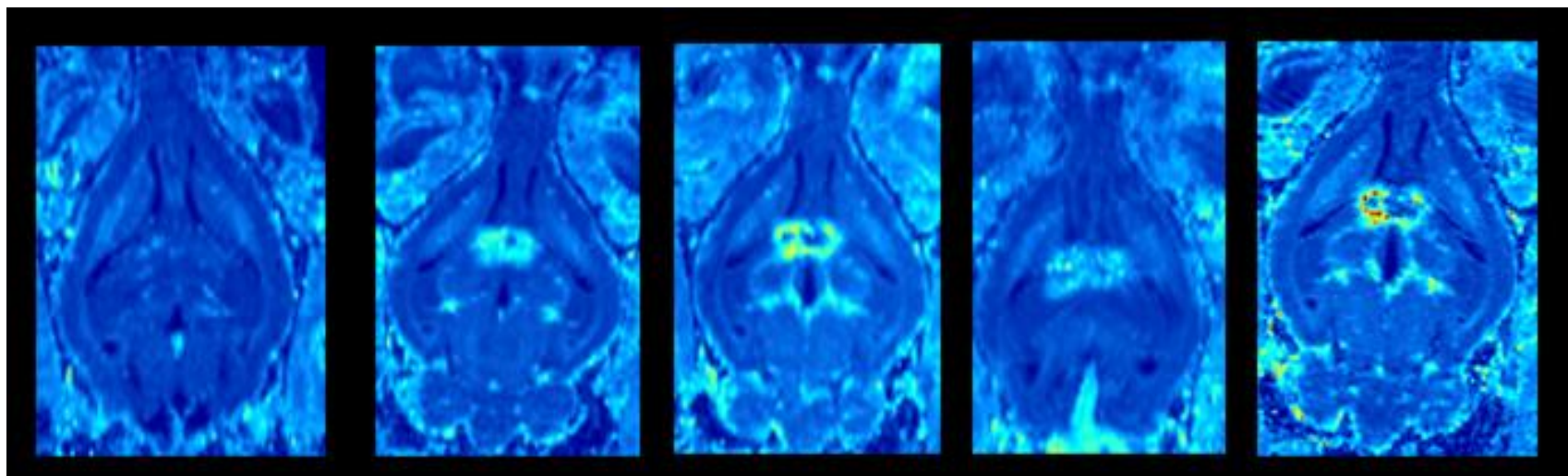


Rabbit Data

Rabbit Brain Model



Probe in Rabbit



Pre-injection

>5 day

12 hour

24 hour

48 hour

Conclusions

- Double treatment method of probe = higher percent conjugations
- Probe effective in mouse model
- Probe effective in preliminary rabbit model tests

Potential Future Research

- Achieve higher conjugation efficiency in probe
- Continue testing probe in rabbit model
- Eventually test probe in more complex animal
- Create human-diagnostic methodology

Bibliography

- Kline E, Bicca M, Viola K, Klein W (2018) The Amyloid- β Oligomer Hypothesis: Beginning of the Third Decade. *Journal of Alzheimer's Disease* **64**, 567-610.
- DiChiara et. al (2017) Alzheimer's Toxic Amyloid Beta Oligomers: Unwelcome Visitors to the Na/K ATPase alpha3 Docking Station. *Yale Journal of Biology and Medicine* **90**,45-61.
- Viola et. al (2014) Towards non-invasive diagnostic imaging of early-stage Alzheimer's disease. *Nature Nanotechnology* 91-98.
- Forny-Germano et. al (2014) Alzheimer's Disease-Like Pathology Induced by Amyloid-Oligomers in Nonhuman Primates. *The Journal of Neuroscience* **34(41)**, 13629–13643
- Bitel et. al (2012) Amyloid- and Tau Pathology of Alzheimer's Disease Induced by Diabetes in a Rabbit Animal Model. *Journal of Alzheimer's Disease* **32**, 291–305

Acknowledgements

Special thank you to **Mrs. Kirsten Viola**, our lab advisor, and **Dr. Klein**, for giving us the opportunity to work in the Klein Lab

Thank you to Dr. Dosch, Dr. Devol, and Dr. Smith for their hard work on the SIR program and IMSAloquium!