

# Nanoscale structure of amyloid- $\beta$ plaques in Alzheimer's disease

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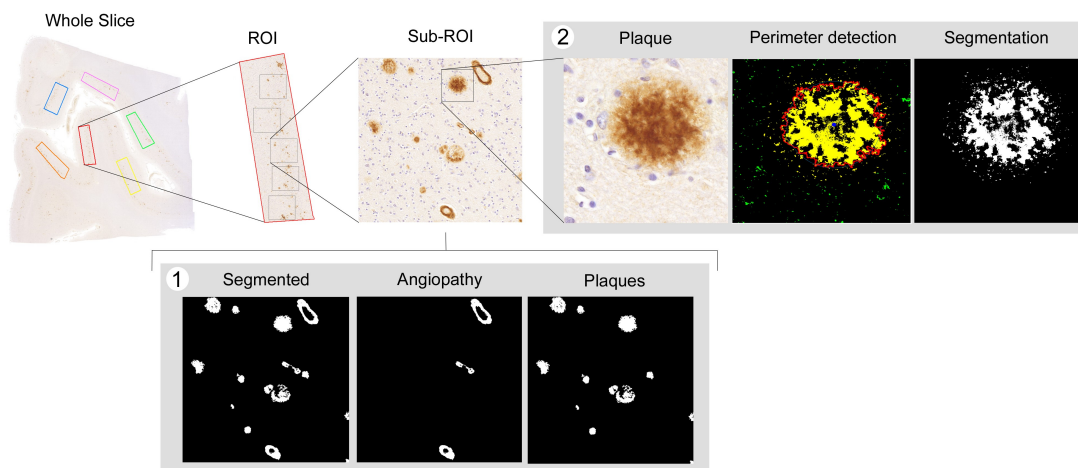
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## SUPPLEMENTAL MATERIAL



**Supplementary Figure S1.** Image processing pipeline. Whole slice scans are obtained and random regions of interest are manually delimited. The application of an in-house algorithm allows two different analyses. 1) Quantification of total A $\beta$  or NAB61 immunoreactivity excluding amyloid angiopathy. 2) Quantification of soluble NAB61+ structures around plaques.

**Supplementary Table S1. Demographic, clinical and genetic data of eoSAD and ADAD patients.**

|  | <b>ADAD<br/>(N =10)</b> | <b>eoSAD<br/>(N =14)</b> | <b>p value</b> |
|--|-------------------------|--------------------------|----------------|
| Gender = M (%)                                   | 7 (70.0)                | 6 (42.9)                 | 0.368          |
| Mean age at onset (mean (SD))                    | 43.80 (6.16)            | 51.36 (3.52)             | <b>0.001</b>   |
| Mean age at death (mean (SD))                    | 54.90 (5.69)            | 60.79 (4.10)             | <b>0.007</b>   |
| Mean disease duration (mean (SD))                | 11.10 (4.41)            | 9.43 (3.25)              | 0.296          |
| <i>APOE</i> $\epsilon$ 4 allele carriers = n (%) | 2 (25.0)*               | 8 (66.7)*                | 0.171          |

\*Calculated without missing data (ADAD n=8 and eoSAD n=12). M: male; SD: standard deviation.

**Supplementary Table S2. Neuropathologic data of eoSAD and ADAD cases.**

| Case #                         | Mutation | Gender | Thal A $\beta$<br>phase | Braak NF<br>stage | CERAD | Age at<br>onset | Age at<br>death | APOE<br>genotype | PMI<br>(h) |
|--------------------------------|----------|--------|-------------------------|-------------------|-------|-----------------|-----------------|------------------|------------|
| <i>PSEN1</i> mutation carriers |          |        |                         |                   |       |                 |                 |                  |            |
| 1                              | V89L     | M      | 5                       | V                 | freq  | 45              | 54              | 23               | 7,5        |
| 2                              | V89L     | M      | 5                       | VI                | freq  | 48              | 57              | 23               | 9.5        |
| 3                              | E120G    | M      | 5                       | VI                | freq  | 34              | 44              | 33               | 5.5        |
| 4                              | M139T    | M      | 5                       | V                 | freq  | 47              | 64              | 33               | 14.7       |
| 5                              | M139T    | M      | 5                       | VI                | freq  | 48              | 57              | 33               | 15.2       |
| 6                              | M139T    | M      | 5                       | VI                | freq  | 45              | 53              | 33               | 5.3        |
| 7                              | M139T    | F      | 5                       | VI                | freq  | 38              | 48              | 23               | 5,25       |
| 8                              | P264L    | F      | 5                       | VI                | freq  | 45              | 56              | 44               | 6          |
| 9                              | P264L    | M      | 5                       | VI                | freq  | 53              | 60              | 34               | 7.2        |
| 10                             | G206D    | M      | 5                       | VI                | freq  | 37              | 44              | 34               | 19.2       |
| Sporadic Early-onset AD        |          |        |                         |                   |       |                 |                 |                  |            |
| 11                             | -        | M      | 4                       | V                 | freq  | 51              | 65              | 44               | 18         |
| 12                             | -        | M      | 4                       | VI                | freq  | 52              | 65              | 33               | 8          |
| 13                             | -        | M      | 4                       | VI                | freq  | 52              | 60              | 44               | 10,25      |
| 14                             | -        | F      | 5                       | VI                | freq  | 51              | 60              | 33               | 5          |
| 15                             | -        | M      | 5                       | VI                | freq  | 46              | 55              | 33               | 4,5        |
| 16                             | -        | F      | 4                       | VI                | freq  | 50              | 63              | 33               | 6,5        |
| 17                             | -        | F      | 5                       | VI                | freq  | 56              | 67              | 44               | 4          |
| 18                             | -        | F      | 5                       | VI                | freq  | 54              | 62              | 44               | 6          |
| 19                             | -        | F      | 5                       | VI                | freq  | 58              | 66              | 43               | 12,5       |
| 20                             | -        | F      | 5                       | VI                | freq  | 52              | 57              | 43               | 4,5        |
| 21                             | -        | F      | 5                       | VI                | freq  | 46              | 56              | 43               | 16,25      |
| 22                             | -        | M      | 5                       | VI                | freq  | 47              | 57              | 43               | 10         |
| 23                             | -        | F      | 5                       | VI                | freq  | 50              | 62              | 33               | 12,6       |
| 24                             | -        | M      | 5                       | VI                | freq  | 54              | 56              | -                | 14,16      |

CERAD: Consortium to Establish a Registry for Alzheimer's Disease; F: female; M: male; NF: neurofibrillary; PMI: post-mortem interval.