

Supplementary Table1: Effect of subcutaneous immunization on total and fibrilar A β in the brains of J20 APP transgenic mice: A β levels for individual mice according to age.

| Control | | | A β | | | MOG | | |
|--------------------------------|--------------------------------------|---------------------------------|----------------------------------|--|--|----------------------------------|---|--|
| Age (months)/Gender | Total brain A β (ng/g) | % Area of ThS | Age (months)/Gender | Total brain A β (ng/g) | % Area of ThS | Age (months)/Gender | Total brain A β (ng/g) | % Area of ThS |
| 12.3 M | 1671 | 2.41 | 11.3 M | 921 | 0.22 | 11.3 M | 163 | 0.28 |
| 13.4 M | 1595 | 3.39 | 11.8 M | 947 | 1.09 | 11.7 M | 21 | 0.11 |
| 13.4 F | 1910 | 3.66 | 11.8 F | 1225 | 1.67 | 12.6 M | 58 | 0.06 |
| 13.8 F | 1250 | 2.27 | 12.6 F | 146 | 1.39 | 12.8 F | 197 | 0.25 |
| 13.8 F | 719 | 1.14 | 13.3 F | 1135 | 0.74 | 12.8 F | 108 | 0.13 |
| 16.5 M | 1125 | 3.45 | 13.4 F | 126 | 0.32 | 13.3 F | 134 | 0.40 |
| 17.1 F | 1596 | 3.72 | 13.4 F | 413 | 0.47 | 13.3 F | 31 | 0.03 |
| | | | 15.0 F | 152 | 0.69 | 13.3 F | 41 | 0.07 |
| | | | | | | 13.6 F | 74 | 0.32 |
| | | | | | | 15.0 F | 47 | 0.13 |
| 14.3\pm0.7 | 1409.4 \pm 152.7 | 2.9 \pm 0.4 | 12.8 \pm 0.4 | 633.3\pm 166.8^a | 0.83 \pm 0.3^a | 13.0 \pm 0.3 | 87.7 \pm 19.2^b | 0.22 \pm 0.1^b |

| MOG -/- | | | GA | | |
|----------------------------------|--|---|----------------------------------|---|--|
| Age (months)/Gender | Total brain A β (ng/g) | % Area of ThS | Age (months)/Gender | Total brain A β (ng/g) | % Area of ThS |
| 13.2 M | 73 | 0.01 | 12.3 M | 118 | 0.01 |
| 13.4 M | 32 | 0.29 | 16.8 M | 267 | 0.27 |
| 13.4 F | 211 | 0.43 | 15.0 F | 271 | 0.22 |
| 15.0 F | 133 | 0.29 | 15.8 F | 490 | 0.27 |
| 15.1 F | 144 | 0.18 | 17.1 F | 885 | 0.50 |
| 15.6 F | 120 | 0.34 | | | |
| 14.3 \pm 0.4 | 118.8 \pm 25.2^b | 0.27 \pm 0.04^c | 15.4 \pm 0.9 | 406.7 \pm 133.6^c | 0.26 \pm 0.1^c |

^a p<0.05 vs. control; ^b p<0.001 vs. control; p<0.05 vs. A β ; ^c p<0.001 vs. control;

Statistical analysis was preformed using the one way ANOVA, Bonferroni test.

Supplementary Table2. Effect of subcutaneous immunization on total and fibrilar A β in the brains of T2576 APP transgenic mice : A β levels for individual mice according to age.

| Control | | | PLP | | |
|----------------------|------------------------------|-------------------|----------------------|---------------------------------|-------------------------------|
| Age (months)/ Gender | Total brain A β (ng/g) | % Area of ThS | Age (months)/ Gender | Total brain A β (ng/g) | % Area of ThS |
| 13.2 M | 831 | 1.58 | 13.3 F | 508 | 0.47 |
| 15.5 M | 1089 | 1.89 | 13.3 F | 651 | 0.99 |
| 16.4 M | 1614 | 2.92 | 15.4 M | 831 | 0.63 |
| 17.9 M | 2390 | 3.88 | 16.4 M | 732 | 0.44 |
| 20.5 F | 2489 | 3.18 | 20.6 M | 637 | 0.83 |
| 16.7±1.2 | 1683 ± 334.1 | 2.67 ± 0.4 | 15.8 ± 1.4 | 672.1 ± 53.6^a | 0.68 ± 0.2^b |

^a p<0.02 vs. control (untreated mice).

^b p<0.002 vs. control. Statistical analysis was preformed using the student's t test .

Supplementary Table 3: Effect of nasal immunization on total and fibrillar A β in the brains of J20 APP transgenic mice: A β levels for individual mice according to age

| Control | | | Control (Age matched) | | |
|---------------------|------------------------------|------------------|-----------------------|------------------------------|------------------|
| Age (months)/Gender | Total brain A β (ng/g) | % Area of ThS | Age (months)/Gender | Total brain A β (ng/g) | % Area of ThS |
| 12.3 M | 1671 | 2.41 | 12.3 M | 1671 | 2.41 |
| 13.4 M | 1595 | 3.39 | 13.4 M | 1595 | 3.39 |
| 13.4 F | 1910 | 3.66 | 13.4 F | 1910 | 3.66 |
| 13.8 F | 1250 | 2.27 | 13.8 F | 1250 | 2.27 |
| 13.8 F | 719 | 1.14 | 13.8 F | 719 | 1.14 |
| 16.5 M | 1125 | 3.45 | | | |
| 17.1 F | 1596 | 3.72 | | | |
| | | | | | |
| 14.3±0.7 | 1409.4 ± 152.7 | 2.9 ± 0.4 | 13.3±0.3 | 1429 ± 233 | 2.6 ± 0.4 |

| GA | | | IVX-908 | | | GA+IVX-908 | | |
|---------------------|------------------------------|-------------------|---------------------|-------------------------------|------------------|---------------------|---------------------------------|--------------------------------|
| Age (months)/Gender | Total brain A β (ng/g) | % Area of ThS | Age (months)/Gender | Total brain A β (ng/g) | % Area of ThS | Age (months)/Gender | Total brain A β (ng/g) | % Area of ThS |
| 12.5 M | 1207 | 2.47 | 13.0 M | 635 | 2.19 | 12.5 M | 158 | 0.12 |
| 12.8 M | 823 | 1.78 | 15.2 M | 802 | 1.67 | 12.5 F | 120 | 0.36 |
| 14.5 F | 968 | 0.71 | 15.2 M | 292 | 0.65 | 12.8 F | 435 | 0.38 |
| 15.1 F | 1068 | 3.29 | 12.7 F | 948 | 2.10 | 13.0 M | 593 | 0.54 |
| | | | 12.9 F | 435 | 0.98 | 13.0 M | 356 | 0.18 |
| | | | 13.0 F | 681 | 1.63 | 13.3 M | 129 | 0.47 |
| | | | 14.8 F | 743 | 1.83 | 13.5 F | 604 | 0.71 |
| | | | | | | 15.8 F | 630 | 0.69 |
| 13.7 ± 0.6 | 1017 ± 81 | 2.06 ± 0.8 | 13.8 ± 0.5 | 648.1 ± 84^a | 1.5 ± 0.2 | 13.3 ± 0.4 | 402.7 ± 70.5^b | 0.48 ± 0.09^c |

^a p<0.02 vs. control; ^b p<0.001 vs. control; ^c p<0.001 vs. control; p<0.05 vs. GA

Statistical analysis was preformed using the one way ANOVA, Bonferroni test.

Supplementary Table 4: Reduction of total and fibrillar A β following GA+IVX-908 and MOG immunization in the brains of aged match J20 APP transgenic mice.

| Group | Age (months) | Total Brain A β (ng/g) | Fibrillar A β %Area ThS | |
|------------------|----------------|------------------------------|-------------------------------|---------|
| Control (n=5) | 13.3 \pm 0.3 | 1429.1 \pm 233 | 2.60 \pm 0.40 | |
| GA+IVX-908 (n=8) | 13.3 \pm 0.4 | 402.7 \pm 70.5 | 0.48 \pm 0.09 | P<0.001 |
| EAE (MOG) (n=8) | 13.3 \pm 0.3 | 86.5 \pm 20.2 | 0.17 \pm 0.05 | P<0.001 |

Statistical analysis was preformed using the one way ANOVA, Bonferroni test.

Supplementary Table 5: Reduction of fibrillar A β following GA+IVX-908 immunization in the brains of age and sex match J20 APP transgenic mice.

| Control | | PLP | |
|----------------|----------------------|---------------|--------------------------------|
| Gender | % Area of ThS | Gender | % Area of ThS |
| M | 2.11 | M | 0.41 |
| M | 2.31 | M | 0.37 |
| M | 1.88 | M | 0.33 |
| M | 2.64 | M | 0.28 |
| M | 1.98 | M | 0.38 |
| F | 2.06 | F | 0.35 |
| F | 2.57 | F | 0.27 |
| F | 2.79 | F | 0.48 |
| F | 2.62 | | |
| | | | |
| Total | 2.3± 0.11 | Total | 0.4 ± 0.03 ^a |

^a p<0.0001 vs. control (untreated mice). Statistical analysis was preformed using the student's t test.