SUPPLEMENTAL FIGURE LEGENDS

Supplemental Figure 1 (S1). SDPM1 and P4D6 recognize low molecular weight $A\beta_{1\text{-}40/42}$ amyloid forms. (A) COS7 cell lysates were made from Mock-, APP WT, and APPswe-transfected cells, as in Figure 1I. Identical amounts of protein lysate were precipitated with biotin-SDPM1, biotin-SDPM2, or control, followed by streptavidin (SA). SA precipitated two endogenously biotinylated proteins from COS7 cells, regardless of transfection, which were blocked by presence of biotinylated SDPM1 or SDPM2 peptide. SDPM1 precipitated tetramer (16kDa) Aβ amyloid from APPswe-transfected cells, which was blotted by $A\beta_{1\text{-}40/42}$ antibody (6E10). (B) The experiment in Fig. 4I and S1A was repeated, only 6E10 was used to precipitate Aβ amyloid. P4D4 blotted low molecular Aβ amyloid in APPswe-transfected cells.

Supplemental Figure 2 (S2). Characterization of SDPM1 and SDPM2 antibody titers and total Thioflavin S and $A\beta_{1\text{-}40/42}$ staining. (A) Antibody titers to SDPM1 and SDPM2 peptides were measured for Mock-, SDPM1-, and SDPM2-immunized APPswePSEN1(A246E) mice that were immunized as Young animals (immunized beginning monthly at 5 mo until 12 mo) or as Old animals (beginning monthly at 12 mo until 18 mo). (B) Total staining signal for Thioflavin S, which binds fibrillar Aβ amyloid plaques, in the cortex or hippocampus was measured using NIH Image software as described in Methods. APPswePSEN1(A246E) mice immunized with SDPM1 showed significant reduction in Thioflavin S staining, regardless of immunization protocol used. (C) Total $A\beta_{1\text{-}40/42}$ staining signal, as assessed in S1B, was reduced in SDPM1-immunized APPswePSEN1(A246E) mice. Errors are SEM for n=10-12 animals per

condition, using 5-6 measurements per animal in A and 12-24 measurements per animal in B and C.

Supplemental Figure 3 (S3). Thioflavin S staining is reduced in the cortex of APPswePSEN1(A246E) mice immunized with SDPM1 with adjuvant. Cortical brain sections from Young (5mo to 12mo) and Old (12mo to 18mo) Mock-, SDPM1-, and SDPM2-immunized mice were compared for staining with Thioflavin S. Bar is 100μm.

Supplemental Figure 4 (S4). Thioflavin S staining is reduced in the brains of APPswePSEN1(A246E) mice immunized with SDPM1 without adjuvant. Brain sections of cortex, hippocampus, and cerebellum from Mock-, SDPM1-, and SDPM2-immunized APPswePSEN1(A246E) mice stained with Thioflavin S shows reduced amyloid plaque burden in the cortex and hippocampus as a result of SDPM1 immunization in Young immunized (5mo to 12mo) animals. Bar is 100μm.

Supplemental Figure 5 (S5). $A\beta_{1\text{-}40/42}$ staining is reduced in the hippocampus of APPswePSEN1(A246E) mice immunized with SDPM1 with adjuvant. Brain sections from Young immunized (5mo to 12mo) and Old immunized (12mo to 18mo) hippocampus from Mock-, SDPM1-, and SDPM2-immunized APPswePSEN1(A246E) mice were compared for $A\beta_{1\text{-}40/42}$ immunostaining. Bar is 100μm.

Supplemental Figure 6 (S6). $A\beta_{1\text{-}40/42}$ staining is reduced in the cortex of APPswePSEN1(A246E) mice immunized with SDPM1 with adjuvant. Brain sections

from Young immunized (5mo to 12mo) and Old immunized (12mo to 18mo) cortex of Mock-, SDPM1-, and SDPM2-immunized mice were compared for $A\beta_{1\text{-}40/42}$ immunostaining. Bar is 100μm.

Supplemental Figure 7 (S7). $A\beta_{1\text{-}40/42}$ staining is reduced in the brains of mice immunized with SDPM1 without adjuvant. Brain sections of cortex, hippocampus, and cerebellum from Mock-, SDPM1-, and SDPM2-immunized mice stained with antibody to $A\beta_{1\text{-}40/42}$ shows reduced plaque burden in the cortex and hippocampus as a result of SDPM1 immunization in Young animals (beginning at 5 mo and analyzed at 12 mo, without adjuvant). Bar is 100μm.

Supplemental Figure 8 (S8). Open field tests of locomotor activity are unchanged by immunization with SDPM1 or SDPM2. Open field tests of motor activity, including total ambulation, ambulation in the center of the cage, ambulation in the periphery of the cage, total fine motor activity (including grooming), and total rearing on hind quarters were measured repeatedly over the course of one day. Activity is reported as number of $1inch^2$ light path crosses per 4 minute trial. APPswePSEN1(A246E) (APP/PS1) mice immunized with SDPM1 or SDPM2 showed no difference from Mock-immunized APPswePSEN1(A246E) mice for any of these measures. Errors are SEM for n=10-12 animals per condition with 10 measurements per condition.

Supplemental Figure 9 (S9). ELISPOT assays for Interleukin 4 (IL4) and Interferon gamma (IFNγ)-positive lymphocytes are unchanged by addition of

SDPM1 or Aβ$_{1-42}$ in SDPM1-immunized APPswePSEN1(A246E) animals. Examples of ELISPOT assays quantitated in Figure 5A. Splenocytes from Young-immunized (Y) or Old-immunized (O) APPswePSEN1(A246E) mice were compared after stimulation with SDPM1, Aβ$_{1-42}$, control (-Peptide), or Concanavalin A (ConA). Number of ELISPOTs was not increased (over –Peptide) by SDPM1 or SDPM2. ConA is a positive control.

Supplemental Figure 10 (S10). Quantitation of immunostaining for GFAP, CD68, and Iba1 in the brains of Mock-, SDPM1-, and SDPM2-immunized APPswePSEN1(A246E) mice. (A) GFAP signal, a marker for astrocytes (that is also increased in reactive astrocytes) was unchanged in SDPM1-immunized APPswePSEN1(A246E) animals. (B) CD68 signal, a marker for activated brain microglia, was significantly reduced in SDPM1-immunized mice. (C) Iba 1 signal, a marker for all brain microglia, was unchanged in SDPM1-immunzied mice. Errors are SEM for n=10-12 animals per condition, with 12-24 measurements per animal.

Supplemental Figure 11 (S11). GFAP immunostaining in the hippocampus of Mock-, SDPM1-, and SDPM2-immunized APPswePSEN1(A246E) mice. GFAP staining was not significantly changed in the hippocampus of SDPM1-immunized mice. Bar is 100μm.

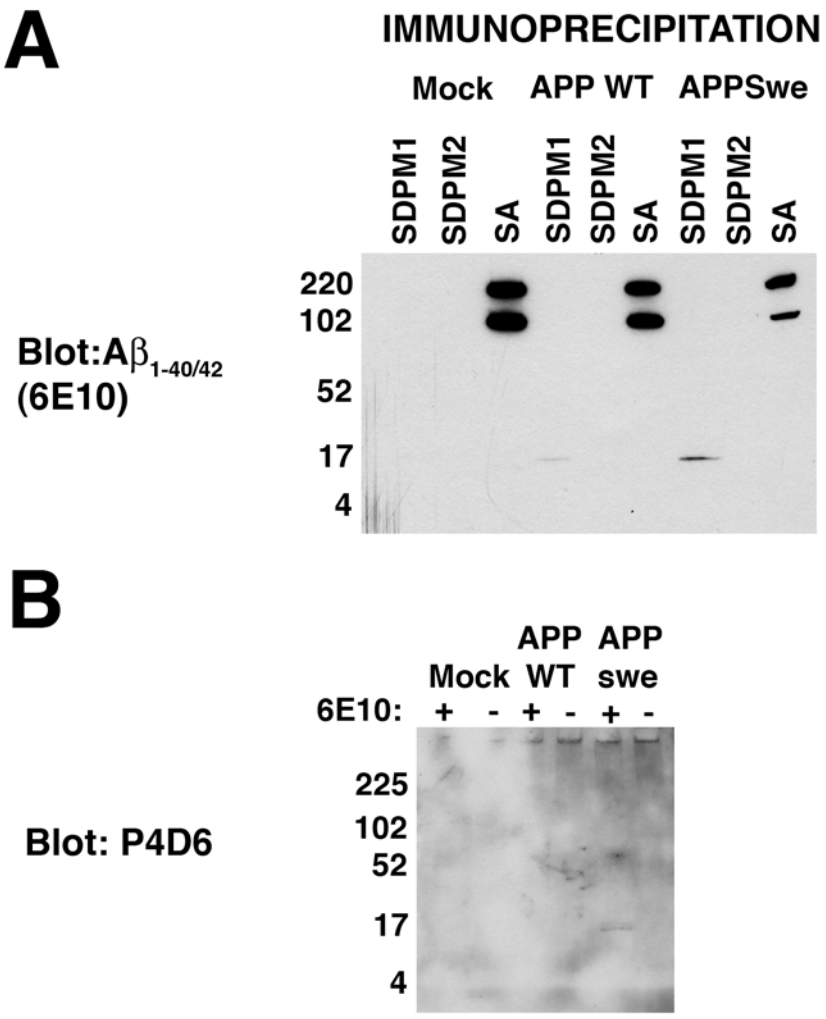
Supplemental Figure 12 (S12). GFAP immunostaining in the cortex of Mock-, SDPM1-, and SDPM2-immunized APPswePSEN1(A246A) mice. GFAP staining was not significantly changed in the cortex of SDPM1-immunized mice. Bar is 100μm.

Supplemental Figure 13 (S13). CD68 immunostaining in the hippocampus of Mock-, SDPM1-, and SDPM2-immunized APPswePSEN1(A246E) mice. CD68 staining was significantly reduced in the hippocampus of SDPM1-immunized mice. Bar is 100μm.

Supplemental Figure 14 (S14). CD68 immunostaining in the cortex of Mock-, SDPM1-, and SDPM2-immunized APPswePSEN1(A246E) mice. CD68 staining was significantly reduced in the cortex of SDPM1-immunized mice. Bar is 100μm.

Supplemental Figure 15 (S15). Iba1 immunostaining in the hippocampus of Mock-, SDPM1-, and SDPM2-immunized APPswePSEN1(A246E) mice. Iba staining was not significantly changed in the hippocampus of SDPM1-immunized mice. Bar is 100μm.

Supplemental Figure 16 (S16). Iba1 immunostaining in the cortex of Mock-, SDPM1-, and SDPM2-immunized APPswePSEN1(A246E) mice. Iba1 staining was not significantly changed in the cortex of SDPM1-immunized mice. Bar is 100μm.



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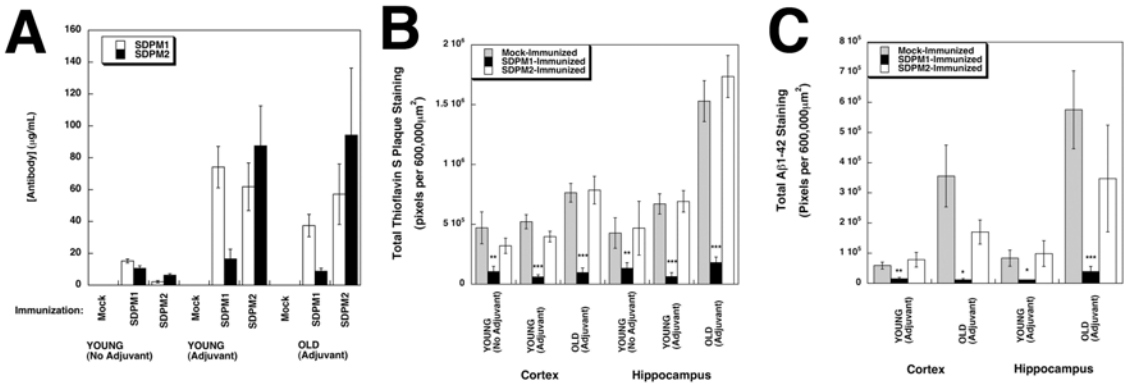

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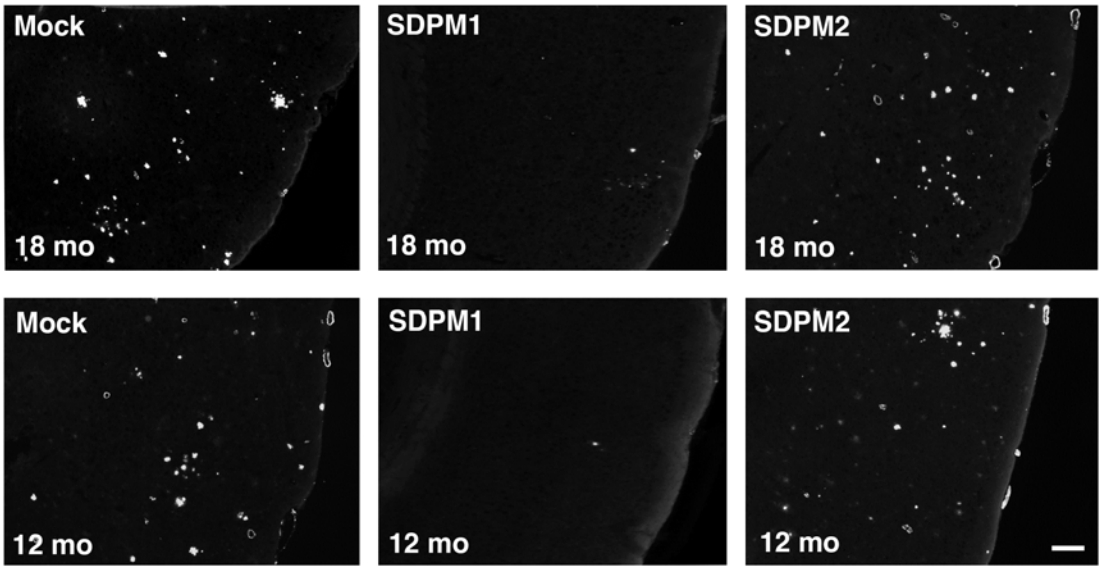

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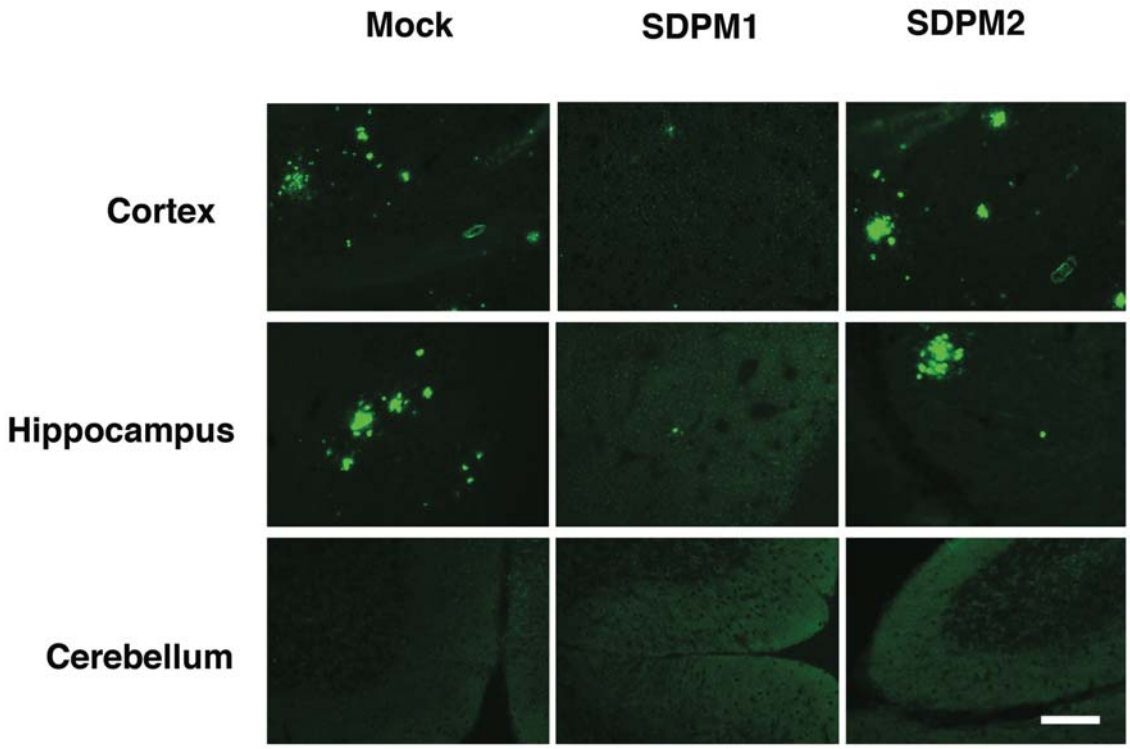

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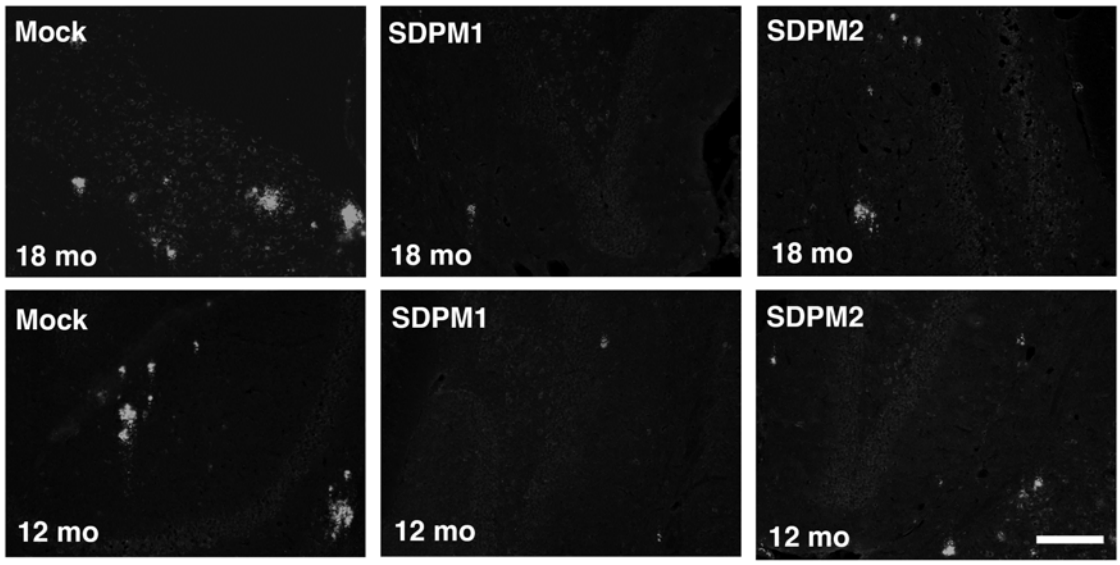

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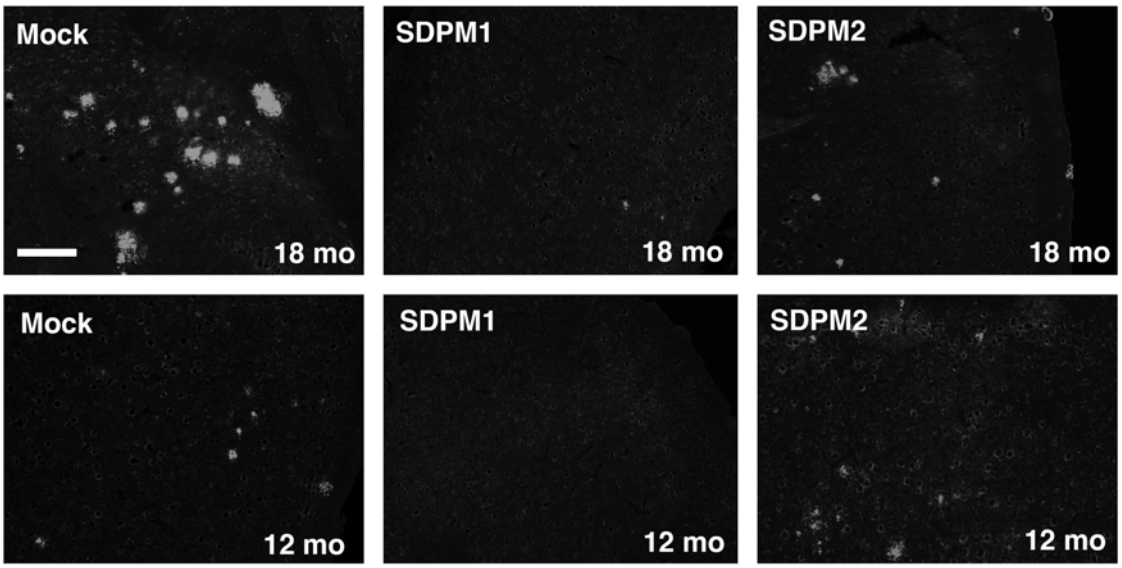

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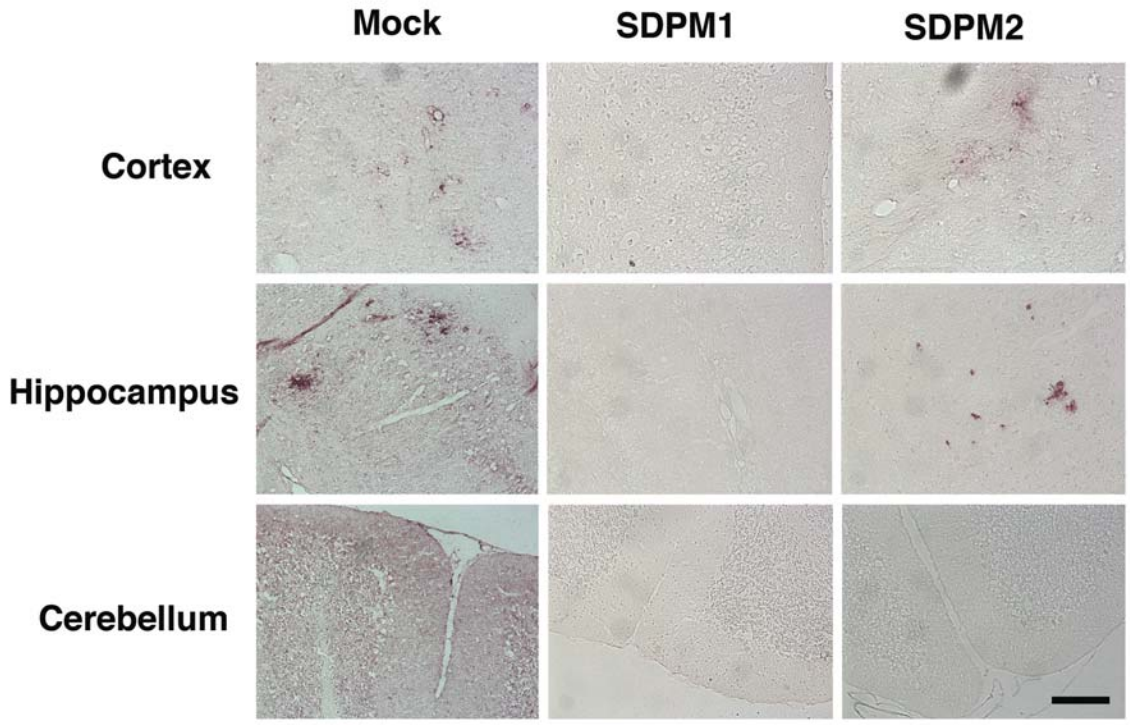

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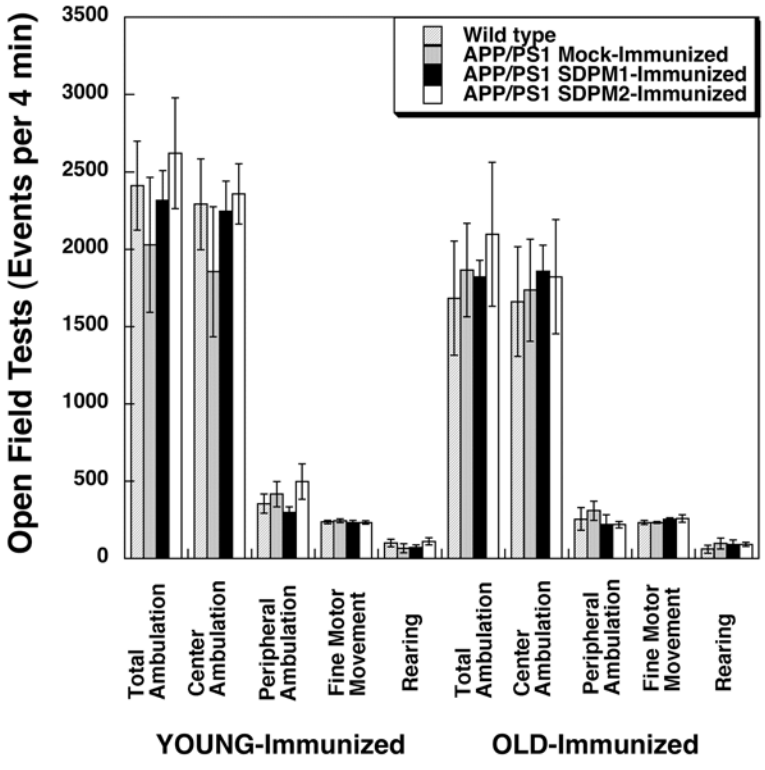

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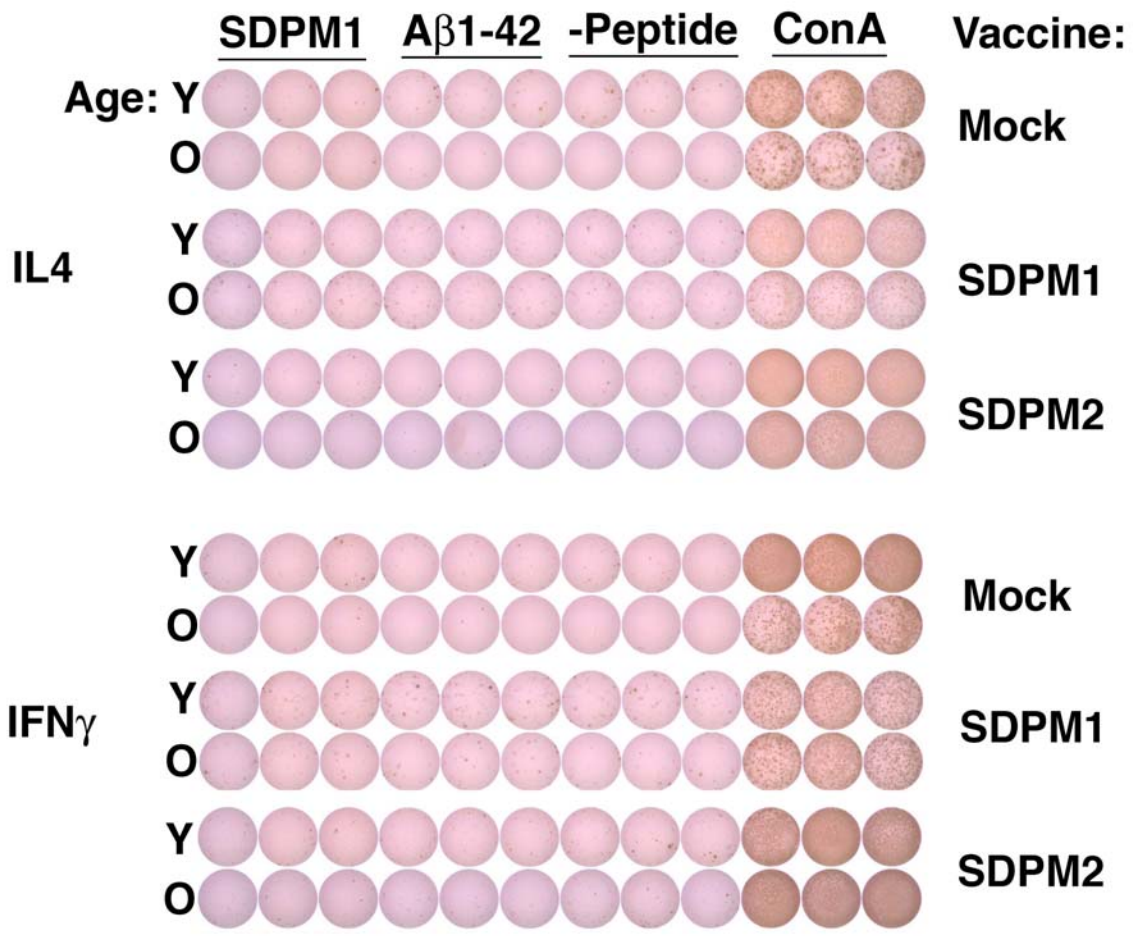

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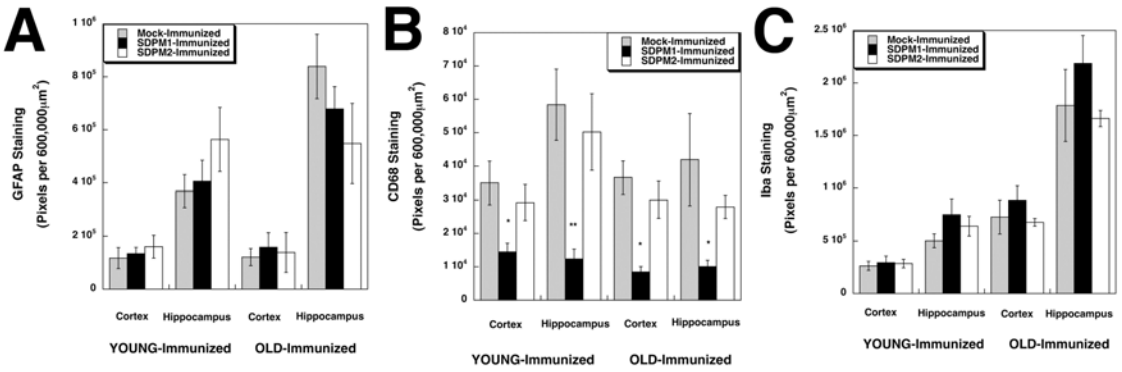

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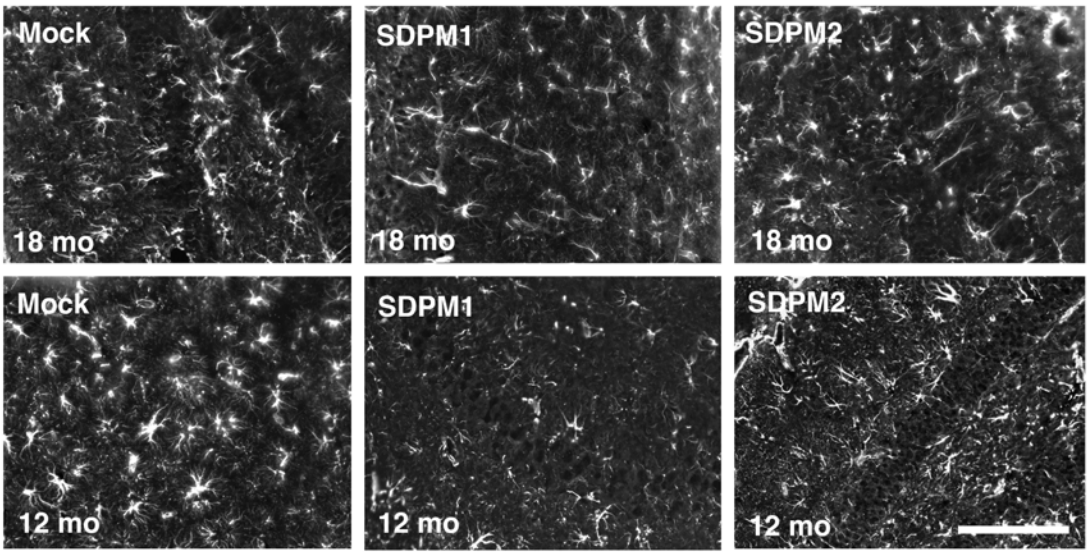

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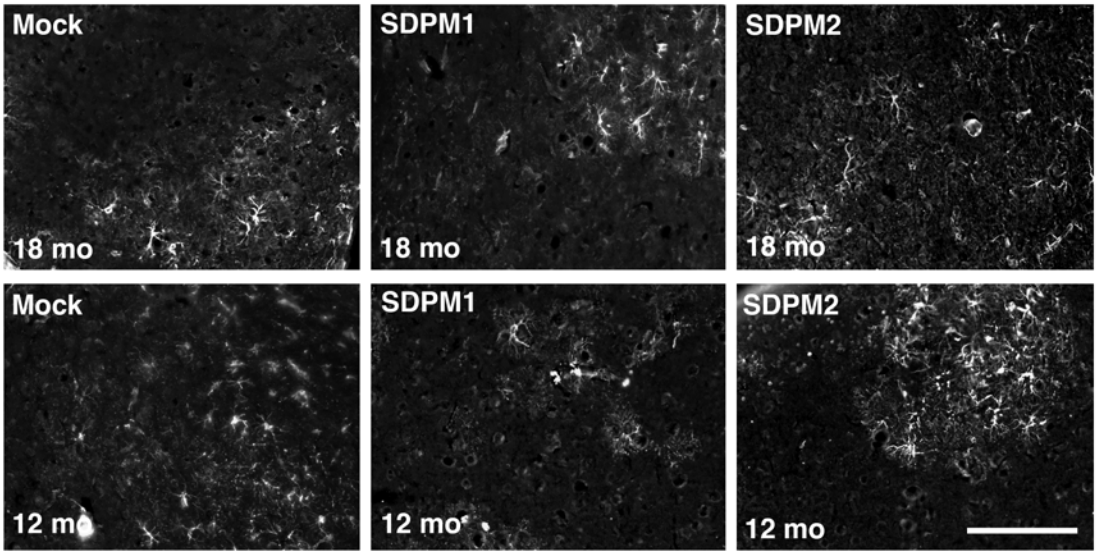

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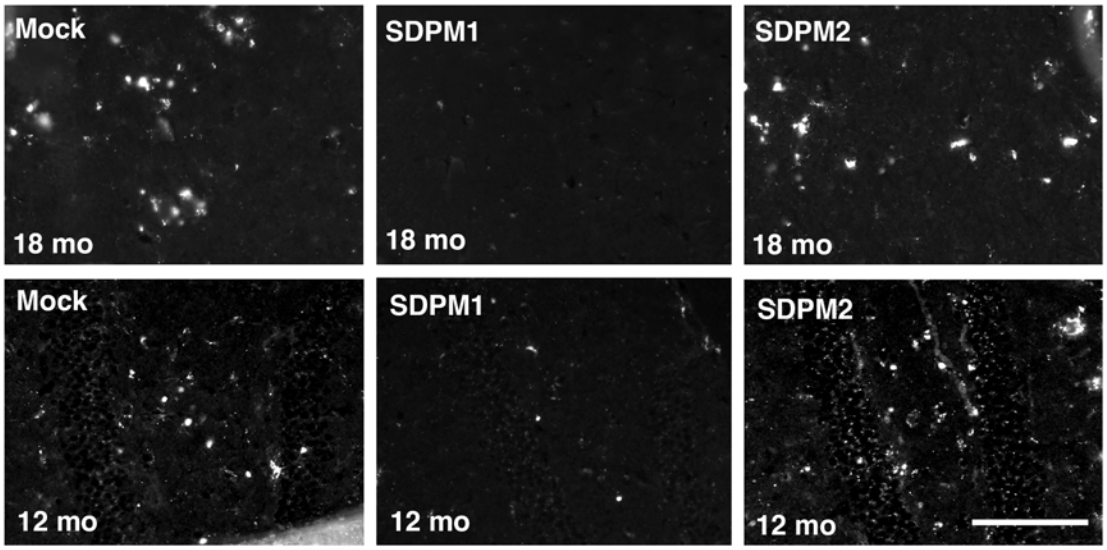

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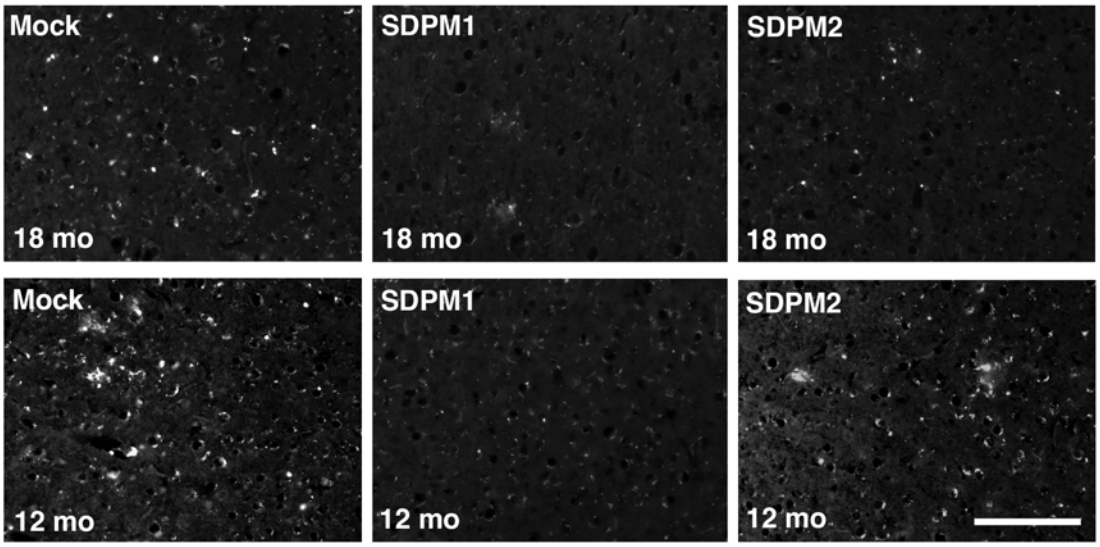

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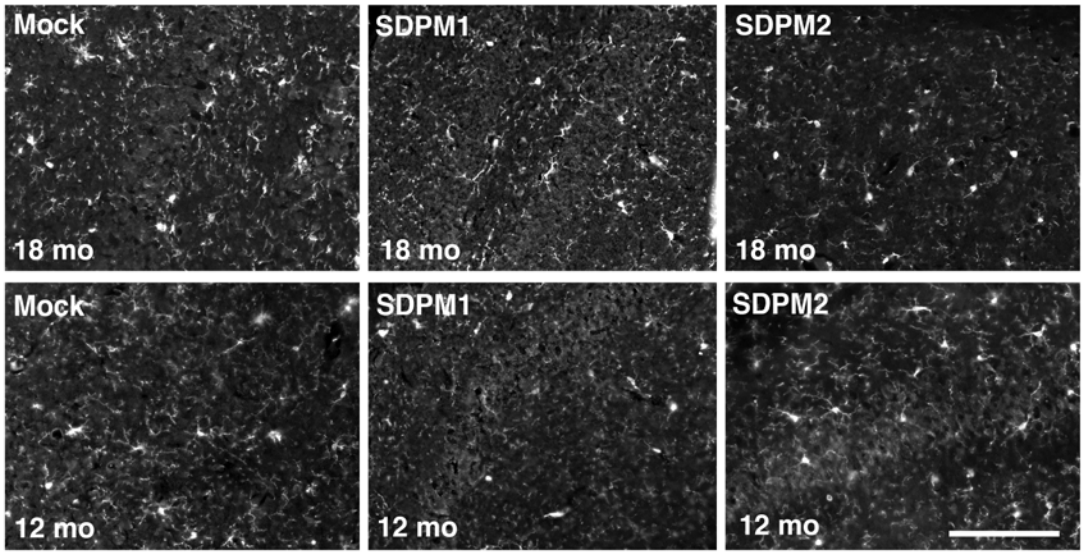

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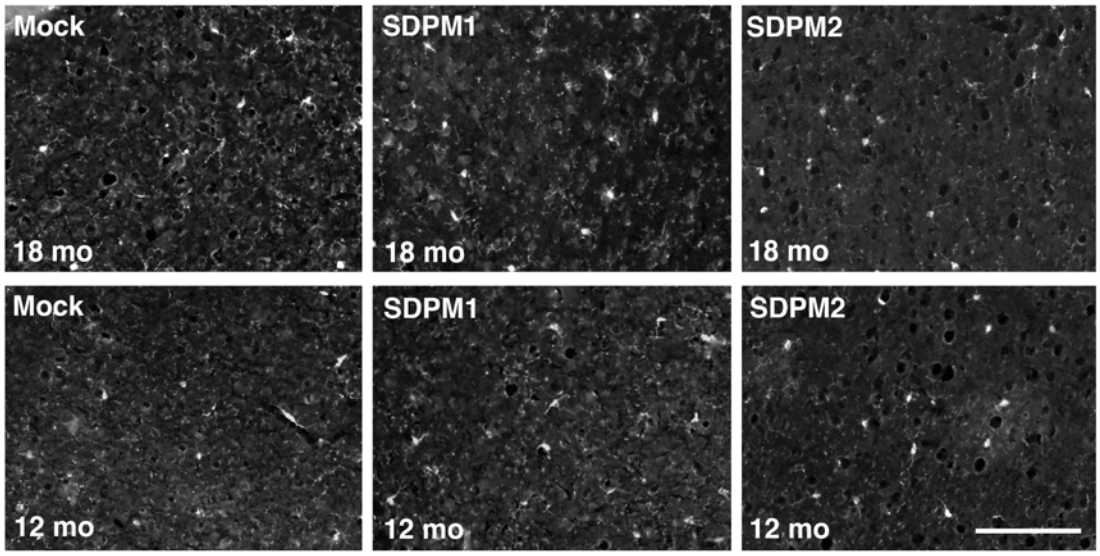

Supplemental Figure 16 (S16)