

Supplementary Material

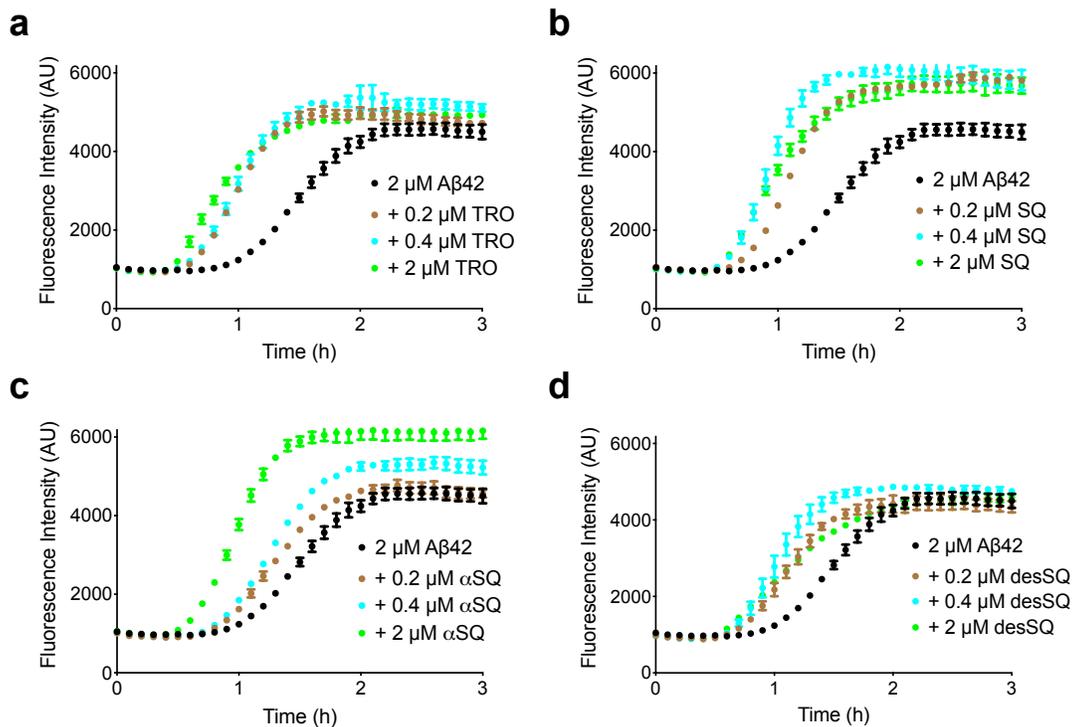


Figure S1. Raw ThT data for the $A\beta_{42}$ aggregation experiments in the presence of increasing concentrations of aminosterols. Kinetic profiles of the aggregation of 2 μ M $A\beta_{42}$ in the absence (black) or presence of 0.2 μ M (brown), 0.4 μ M (cyan) and 2 μ M (green) of TRO (a), SQ (b), α SQ (c) and desSQ (d). Data represent mean \pm standard error of the mean (s.e.m.) of three technical replicates.

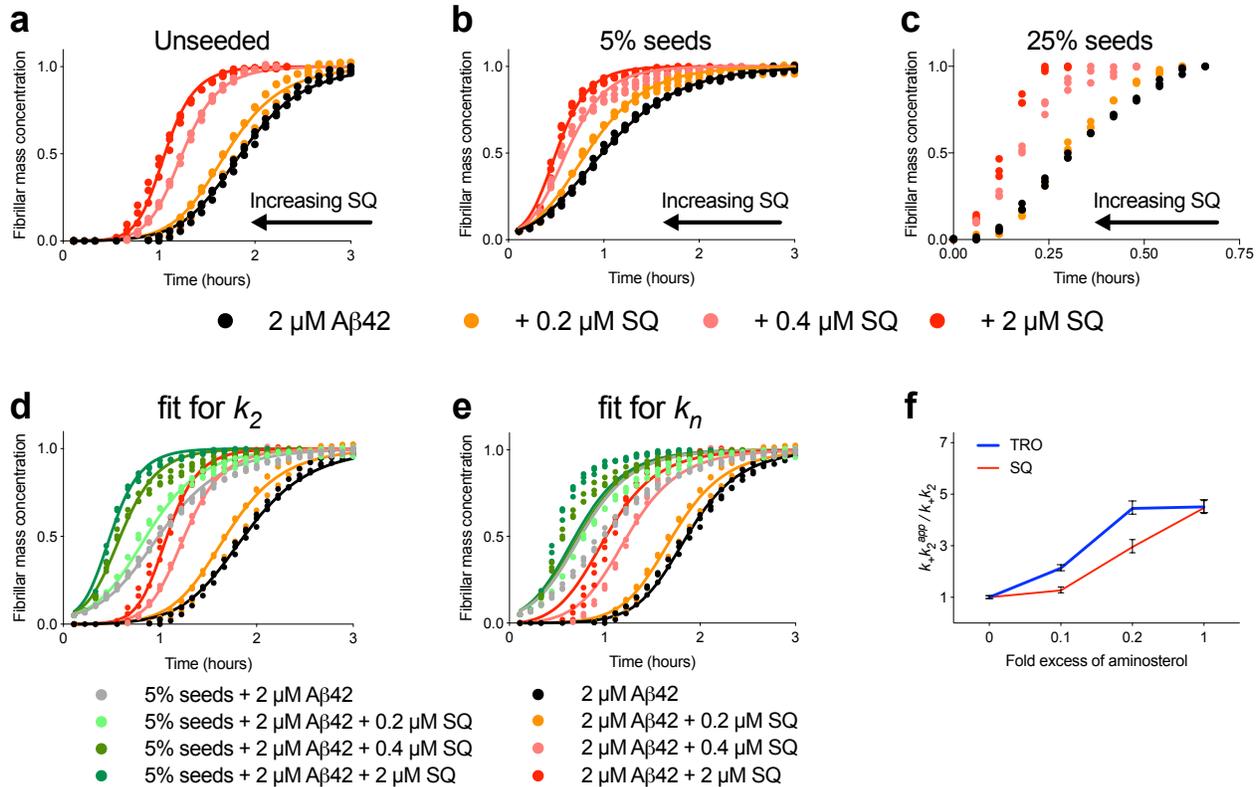
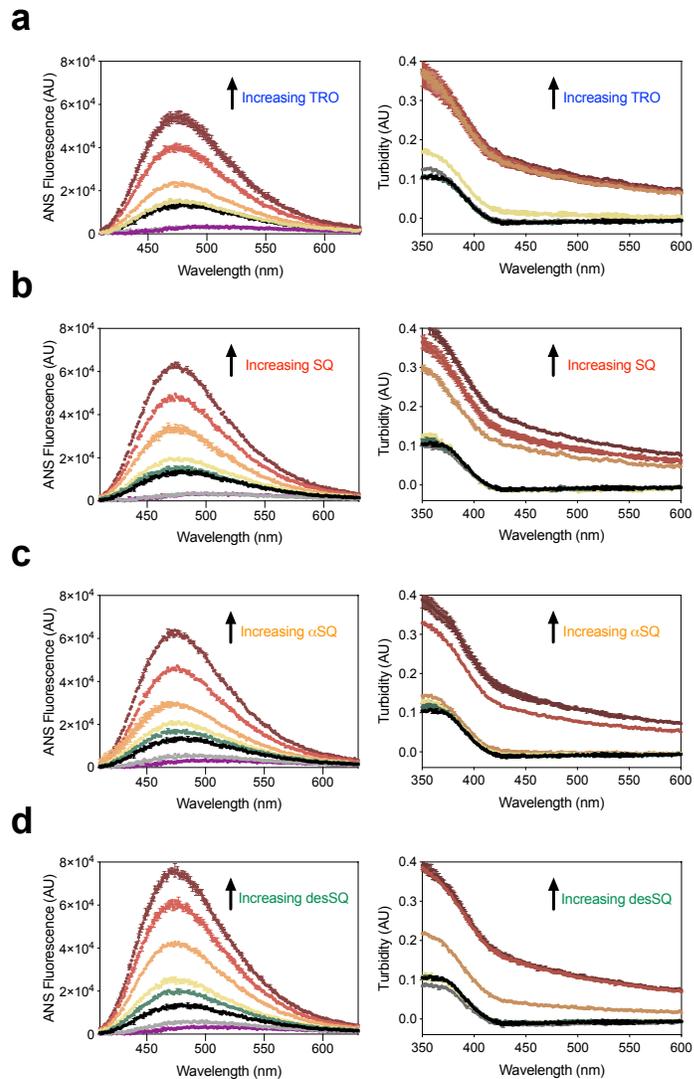


Figure S2. Squalamine modifies the aggregation of $A\beta_{42}$ in a similar manner as trodusquemine.

(a) Kinetic profiles of the aggregation of $2 \mu\text{M } A\beta_{42}$ in the absence (black) or presence of squalamine at ratios of $A\beta_{42}$:squalamine of 10:1, 5:1, and 1:1 (light to dark red, ranging from 0.2 to $2 \mu\text{M}$). Solid lines indicate theoretical predictions based on kinetic fitting (see Results); data are well-described by varying the rates associated with just the secondary nucleation pathway ($k+k_2$). (b) Kinetic profiles of the aggregation of $2 \mu\text{M } A\beta_{42}$ in the presence of 5% fibril seeds and in the absence (black) or presence of squalamine at ratios of 10:1, 5:1, and 1:1 (light to dark red). Solid lines indicate theoretical predictions based on kinetic fitting (see Results); data are well-described by varying the rates associated with just monomer-dependent secondary nucleation (k_2). (c) Kinetic profiles of the aggregation of $2 \mu\text{M } A\beta_{42}$ in the presence of 25% fibril seeds and in the absence (black) or presence of squalamine at ratios of 10:1, 5:1, and 1:1 (light to dark red). (d) As was observed for trodusquemine, the unseeded and 5% seeded data were well-described for the global modification of k_2 , while global fits for k_n were poor (e). (f) Dependency of the apparent reaction rate constants of secondary pathways ($k+k_2$) on increasing concentrations of squalamine (red). Data represent mean \pm s.e.m. of three technical replicates. Shown for comparison are the rates for trodusquemine (blue, previously published in Limbocker et al., 2019). These measurements were carried out alongside a comparison of the effect of trodusquemine on $A\beta_{42}$ aggregation, and the aggregation traces in the absence of squalamine therefore are the same data as previously published (Limbocker et al., 2019).



- 5 μM oligomers • + 5 μM molecule • + 12.5 μM molecule • + 25 μM molecule
- + 37.5 μM molecule • + 50 μM molecule • 50 μM molecule • ANS

Figure S3. Aminosterols increase the size and hydrophobicity of αS oligomers. The effects of aminosterols (0-10 fold excesses, represented in different colors) on the physicochemical properties of oligomers comprised of αS were monitored using ANS binding (left panels) and turbidity absorbance (right panels) to measure hydrophobicity and size, respectively, for trodusquemine (**a**; blue), squalamine (**b**; red), αSQ (**c**; orange) and desSQ (**d**; green). Measurements of ANS in the absence (purple traces) and presence of 50 μM of each molecule (grey traces), corresponding to the highest concentration tested in vitro, are shown for reference. Data represent mean \pm s.e.m. of two technical replicates.

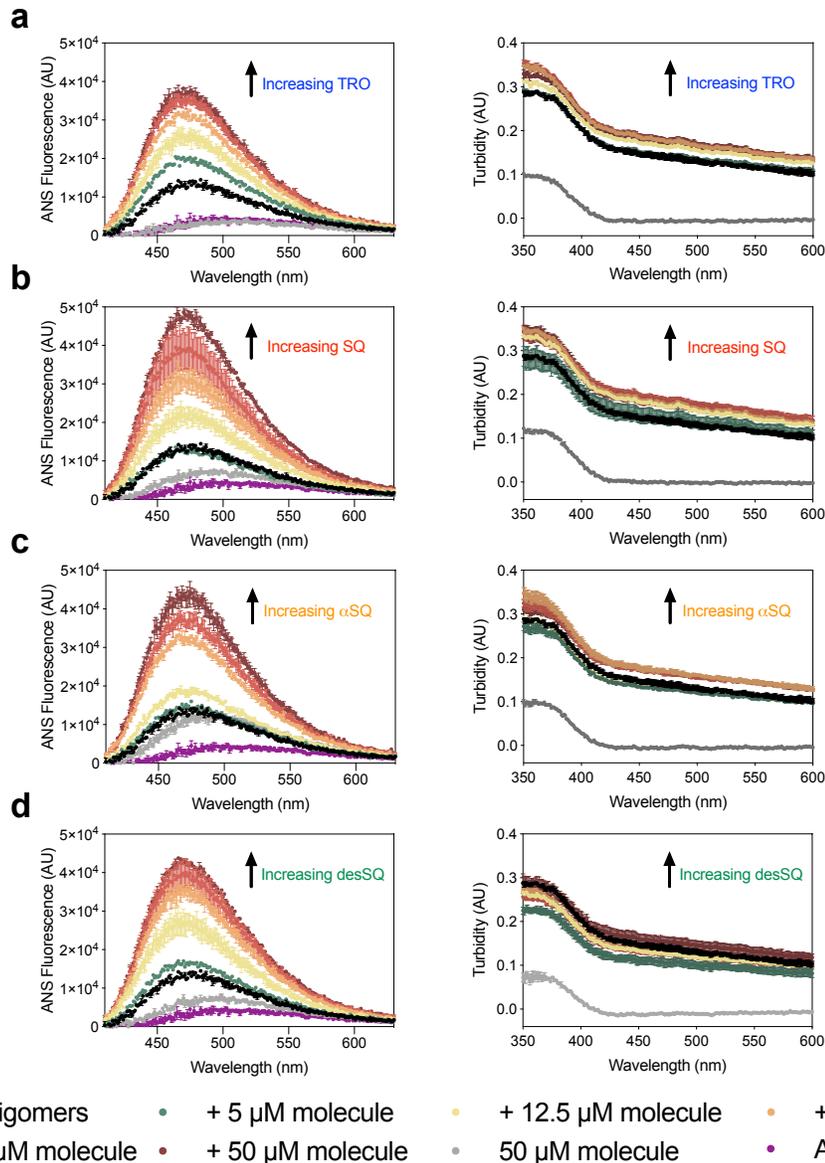


Figure S4. Aminosterols increase the size and hydrophobicity of HypF-N oligomers. The effects of aminosterols (0-10 fold excesses, represented in different colors) on the physicochemical properties of oligomers were monitored using ANS binding (left panels) and turbidity absorbance (right panels) to measure hydrophobicity and size, respectively, for trodusquemine (**a**; blue), squalamine (**b**; red), αSQ (**c**; orange) and desSQ (**d**; green). Measurements of ANS in the absence (purple traces) and presence of 50 μM of each molecule (grey traces), corresponding to the highest concentration tested in vitro, are shown for reference. Data represent mean \pm s.e.m. of two technical replicates.

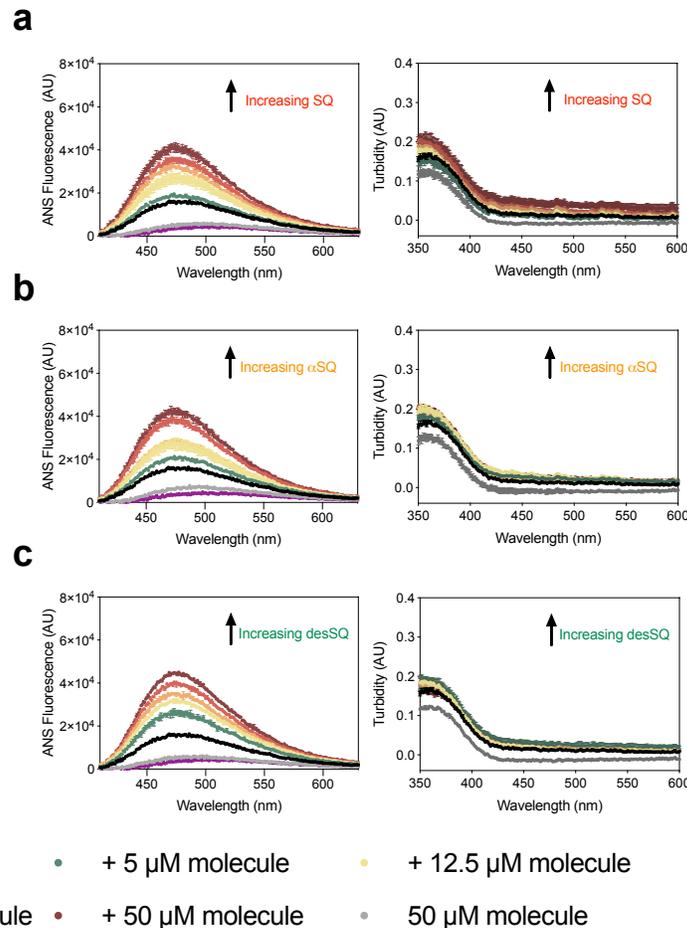


Figure S5. Aminosterols increase the size and hydrophobicity of $\text{A}\beta_{40}$ stabilized by Zn^{2+} . The effects of aminosterols (0-10 fold excesses, represented in different colors) on the physicochemical properties of oligomers comprised of $\text{A}\beta_{40}$ were monitored using ANS binding (left panels) and turbidity absorbance (right panels) to measure hydrophobicity and size, respectively, for squalamine (a; red), αSQ (b; orange) and desSQ (c; green). Measurements of ANS in the absence (purple traces) and presence of 50 μM of each molecule (grey traces), corresponding to the highest concentration tested in vitro, are shown for reference. Data represent mean \pm s.e.m. of two technical replicates. These measurements were carried out alongside a comparison of the effect of trodusquemine on $\text{A}\beta_{40}$ oligomers, for which highly similar results as those observed here with these three aminosterols were obtained (Limbocker et al., IJMS, 2020a).