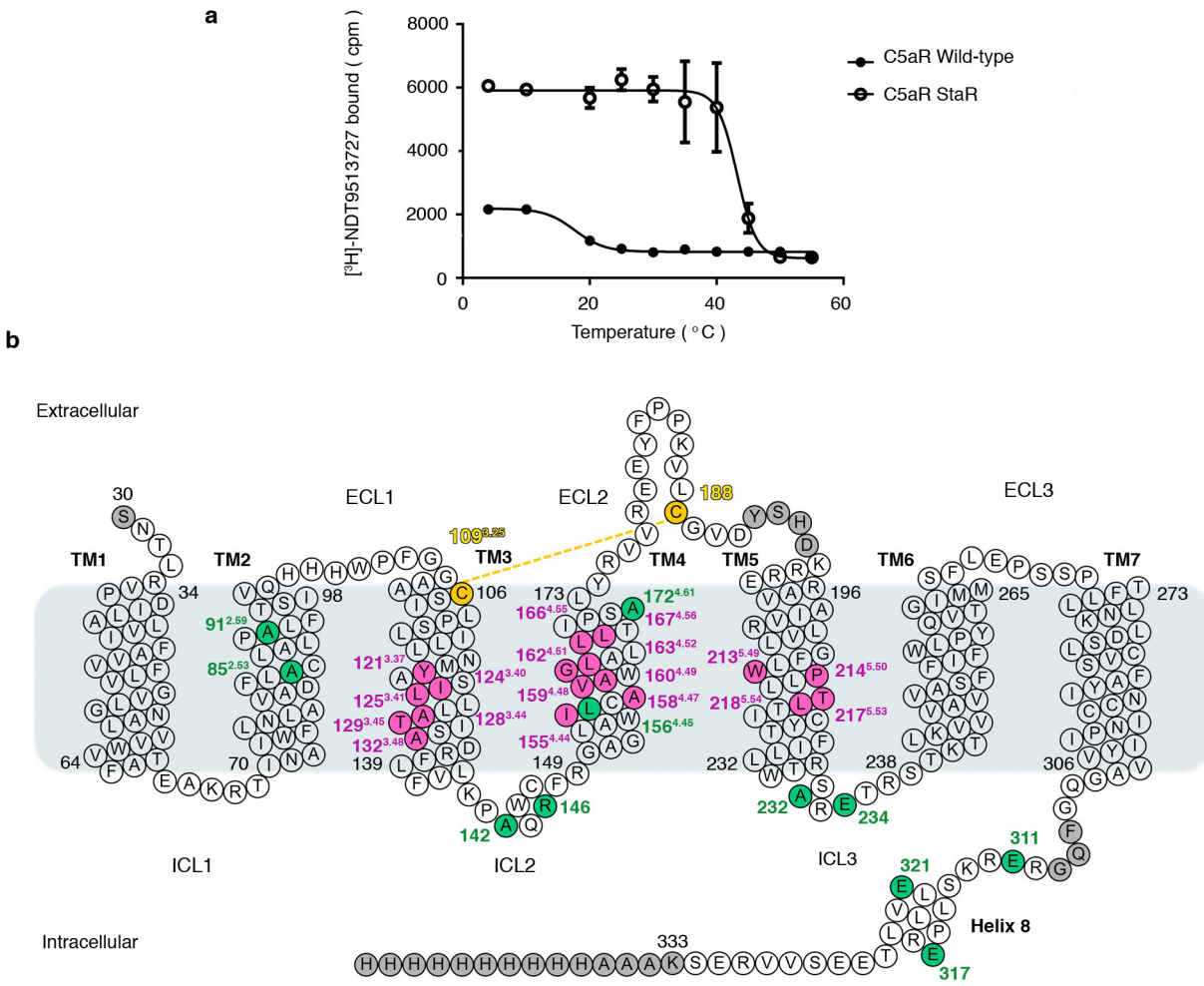


**Extended Data Figure 1 | Comparison of wild-type and thermostabilized C5aR1 and the C5aR1 StaR crystallization construct in schematic representation. a**, Thermal stability of C5aR1 measured using [$^3$H]NDT9513727 binding after solubilization in DDM. Wild-type full-length C5aR1 (closed circles) has a melting temperature ($T_m$) of 18 °C ± 1.05 °C, and C5aR1 StaR full-length (open circles) has a $T_m$ of 44 °C ± 0.7 °C. Data are mean ± s.d. from 3 independent experiments. **b**, C5aR1 StaR crystallization construct in schematic snake plot representation. Thermostabilizing mutations (green) are: S85A, I91A, I142A, N146R, L156A, F172A, R232A, A234E, L311E, S317E and N321E. Residues forming the NDT9513727 pocket are coloured pink. Disordered residues in the structure are grey. The disulfide bond between Cys109$^{3.25}$ and Cys188 is denoted by a dashed yellow line. **c**, Multiple sequence alignment of human, chimpanzee, orangutan, gorilla, macaque, gerbil, cattle, mouse, rat and trout C5aR1 across TM5. The asterisk indicates the tryptophan residue at Ballesteros–Weinstein position 5.49 that is crucial for the interaction of the small-molecule NDT9513727 with C5aR1.

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