

Fig. 1: Schematic presentation of the signal cascade of the NLRP3 activation

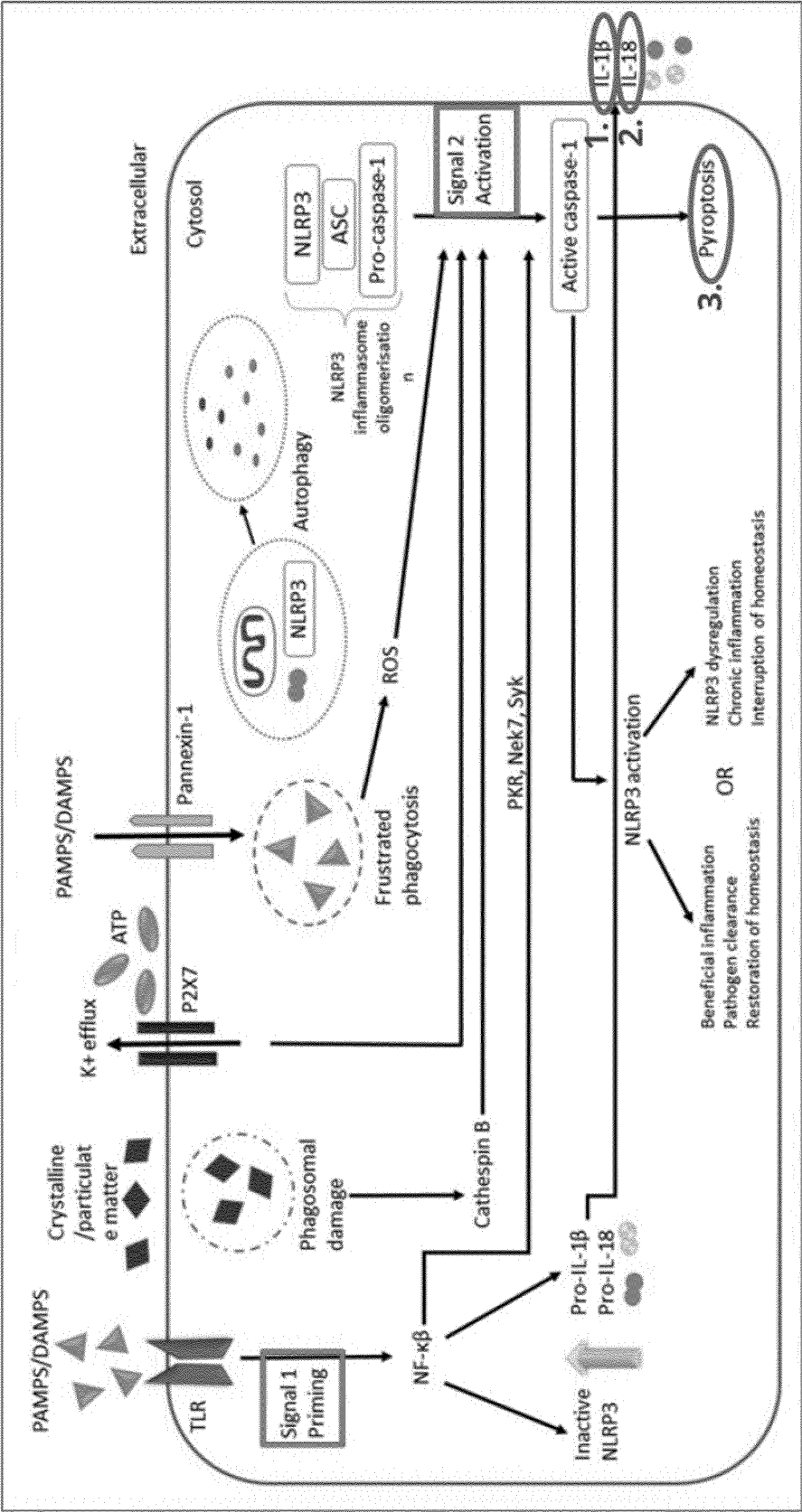


Fig. 2: Single concentration efficacy screen of human NLRP3-specific antisense oligonucleotides in THP-1 cells – first screening
Fig. 2)

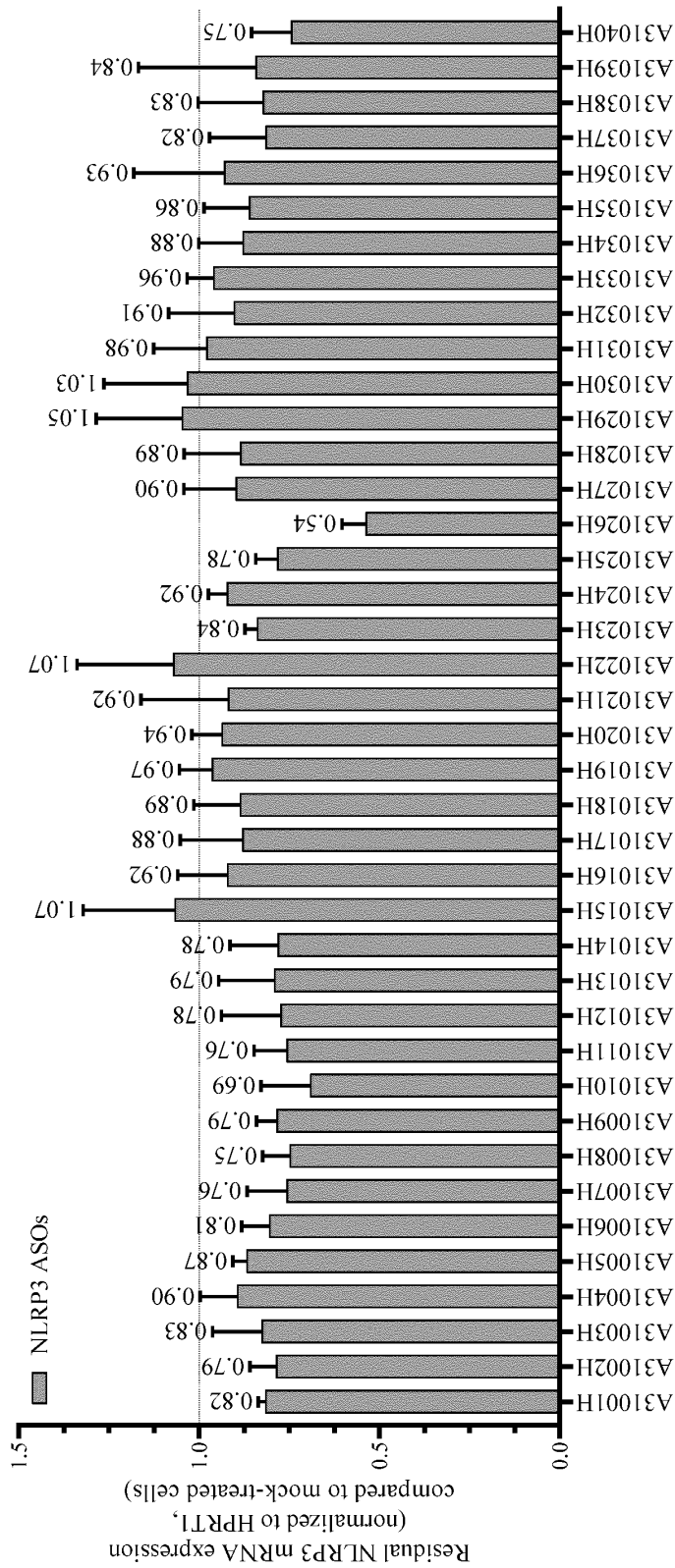


Fig. 2 continued)

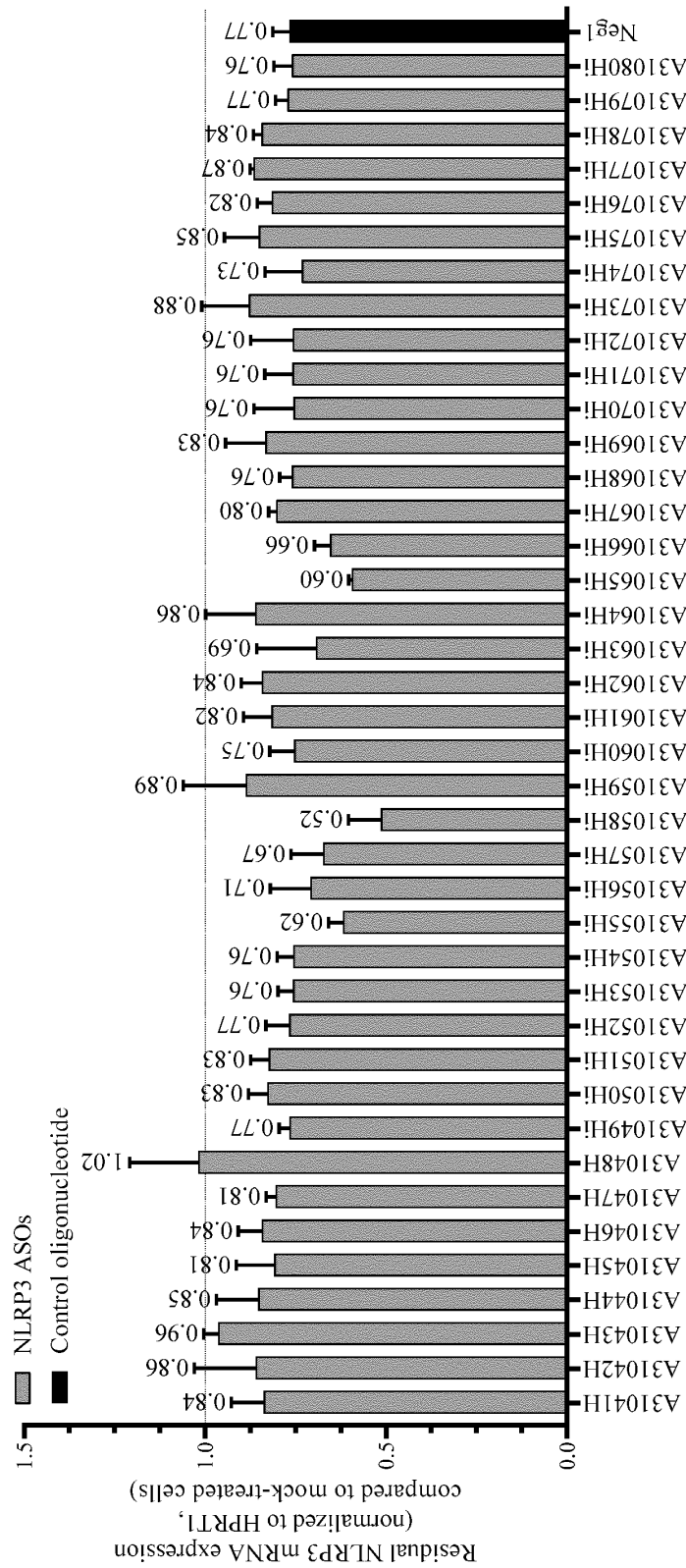


Fig. 3: Single concentration efficacy screen of human NLRP3-specific antisense oligonucleotides in U87MG cells – first screening
Fig. 3)

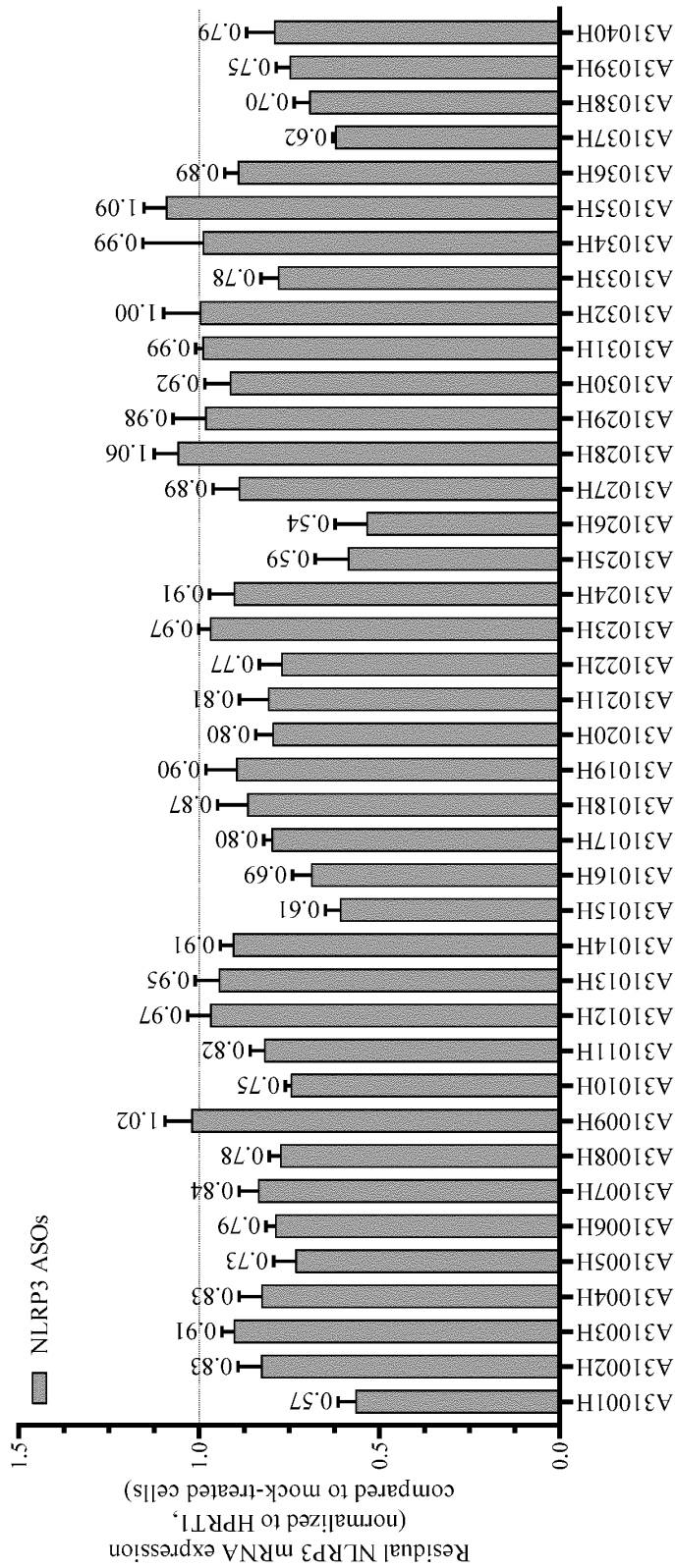


Fig. 3 continued)

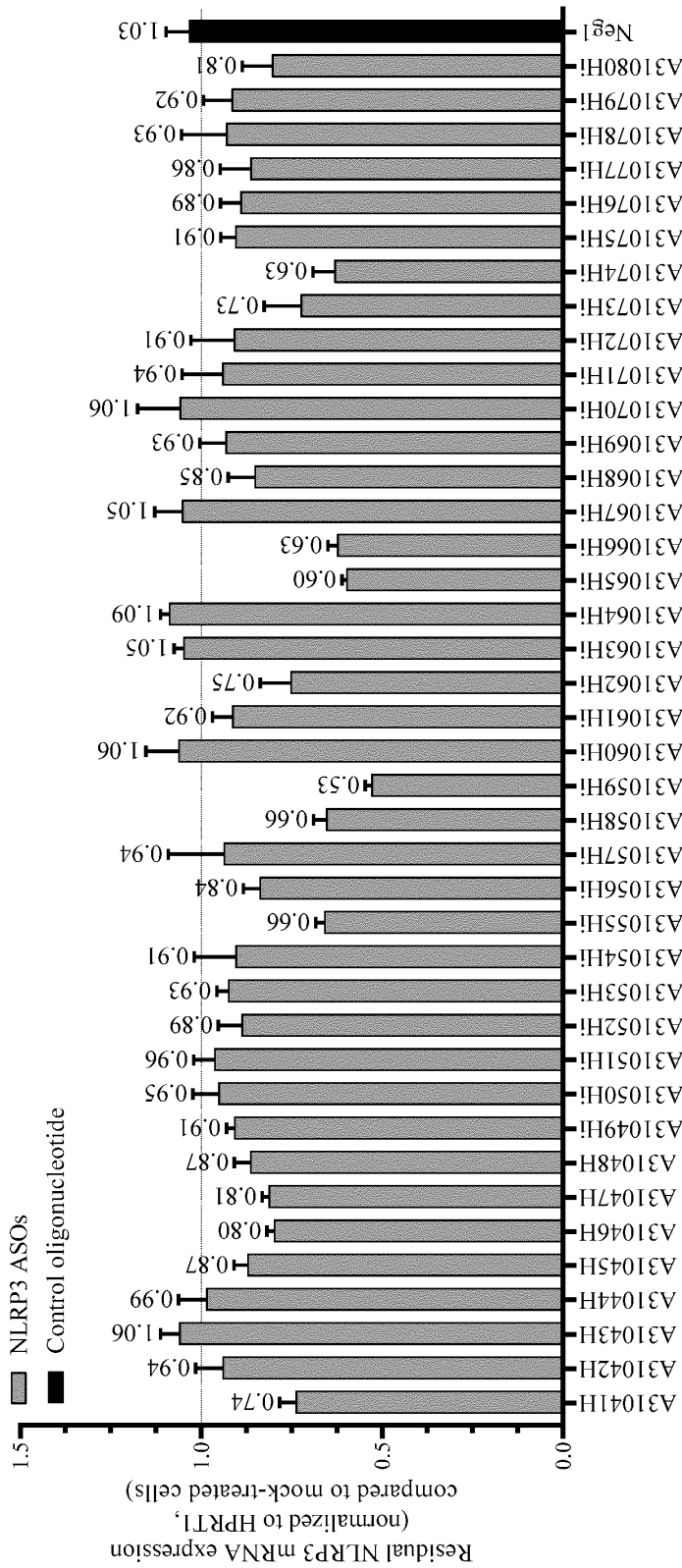


Fig. 4: Single concentration efficacy screen of human NLRP3-specific antisense oligonucleotides in PBMC-derived macrophages – first screening

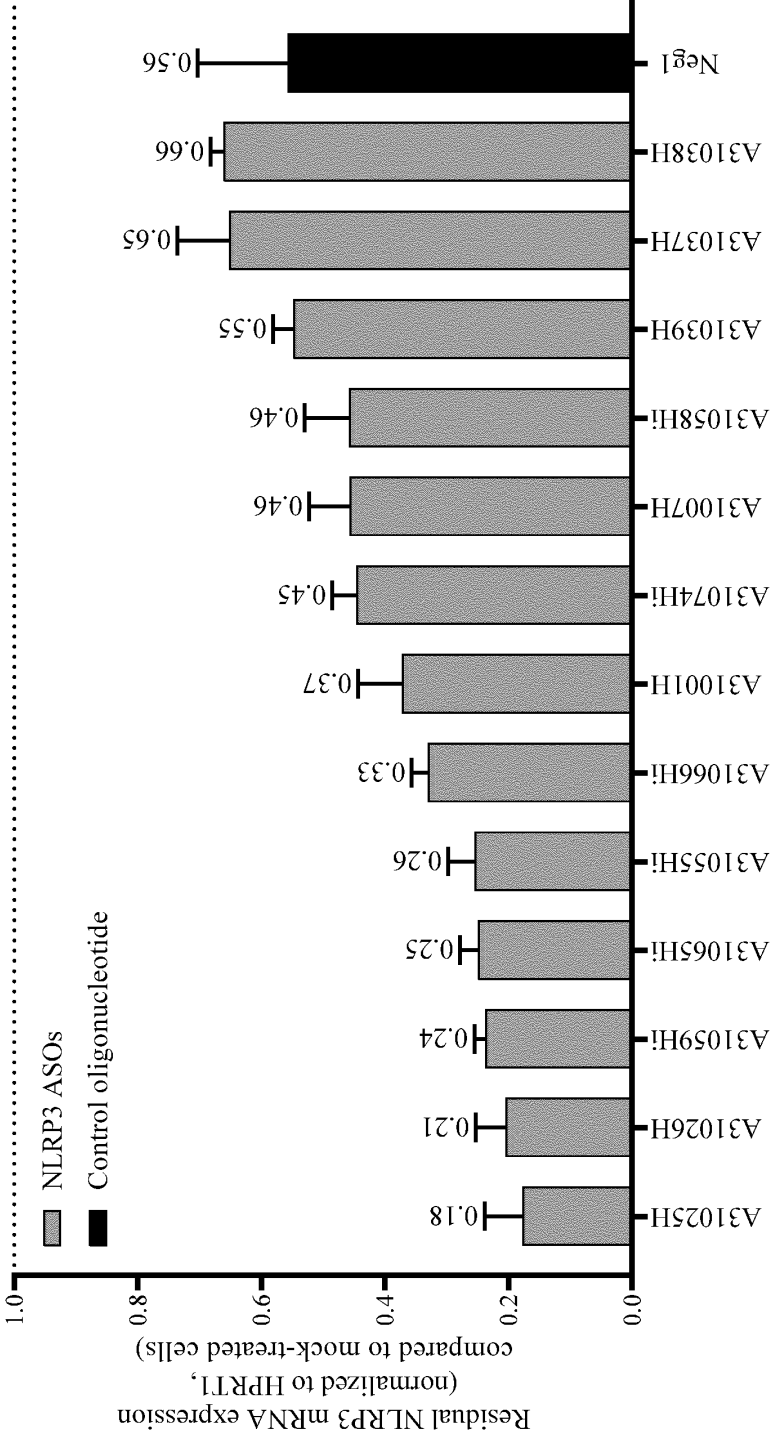


Fig. 5: Single concentration efficacy screen of human NLRP3-specific ASOs in U87MG cells – second screening

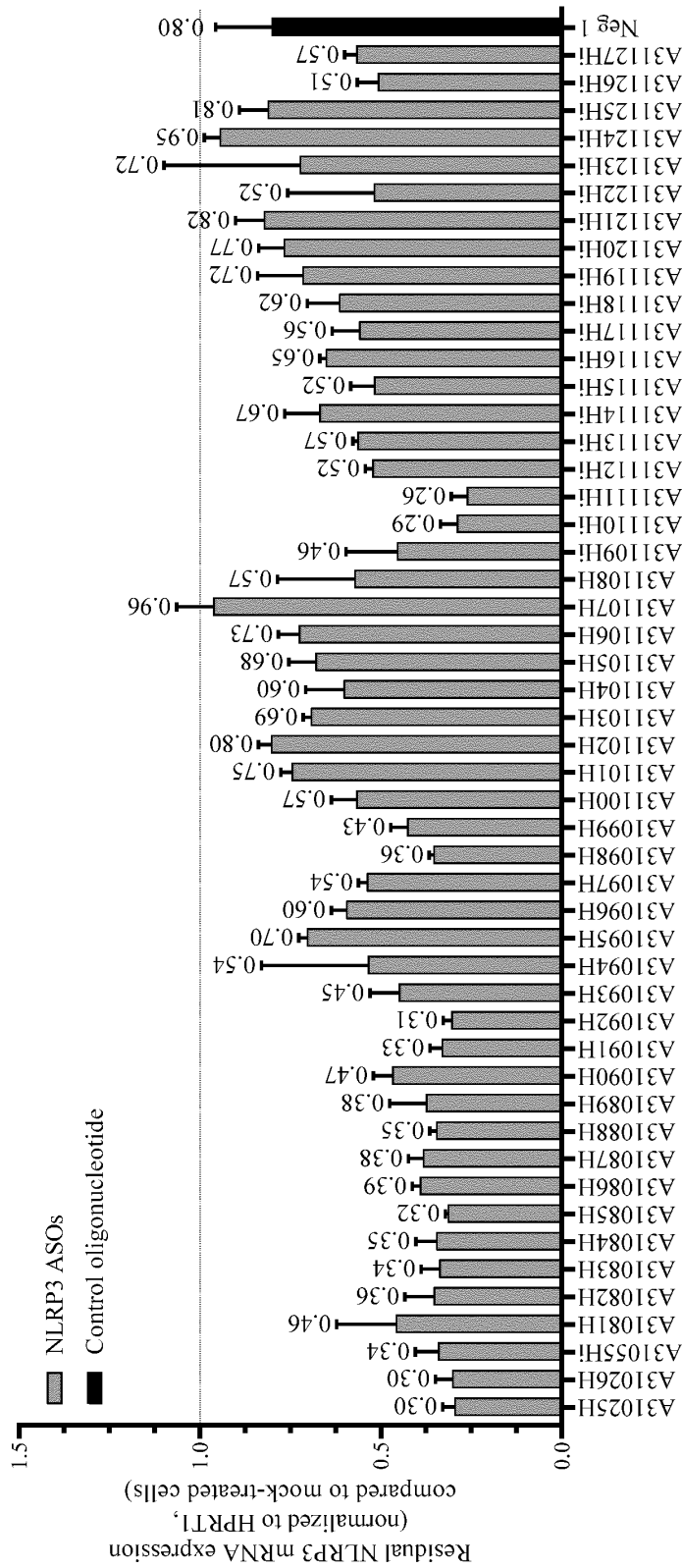


Fig 6: Single concentration efficacy screen of human NLRP3-specific ASOs in PBMC-derived macrophages – second screening

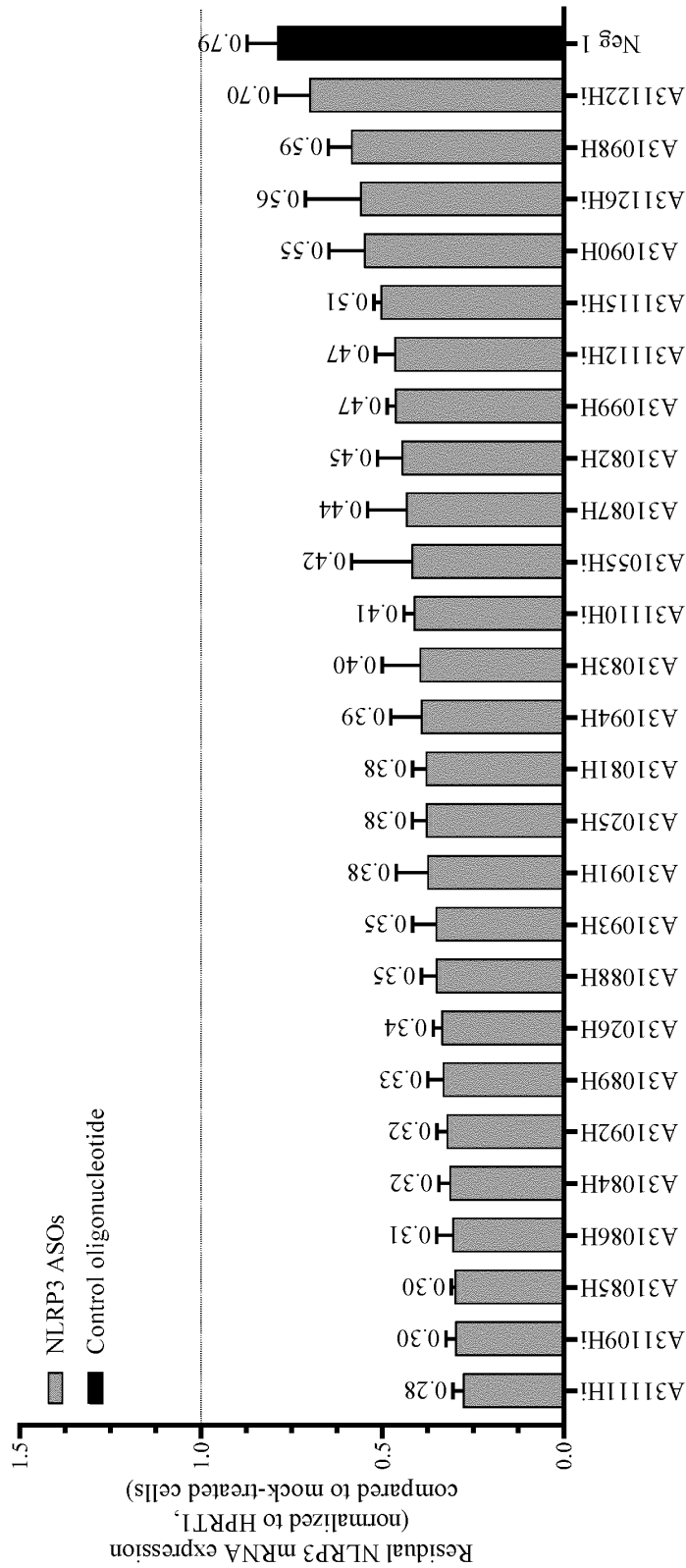


Fig. 7: Concentration response curve of selected human NLRP3-specific ASOs in human PBMC-derived macrophages

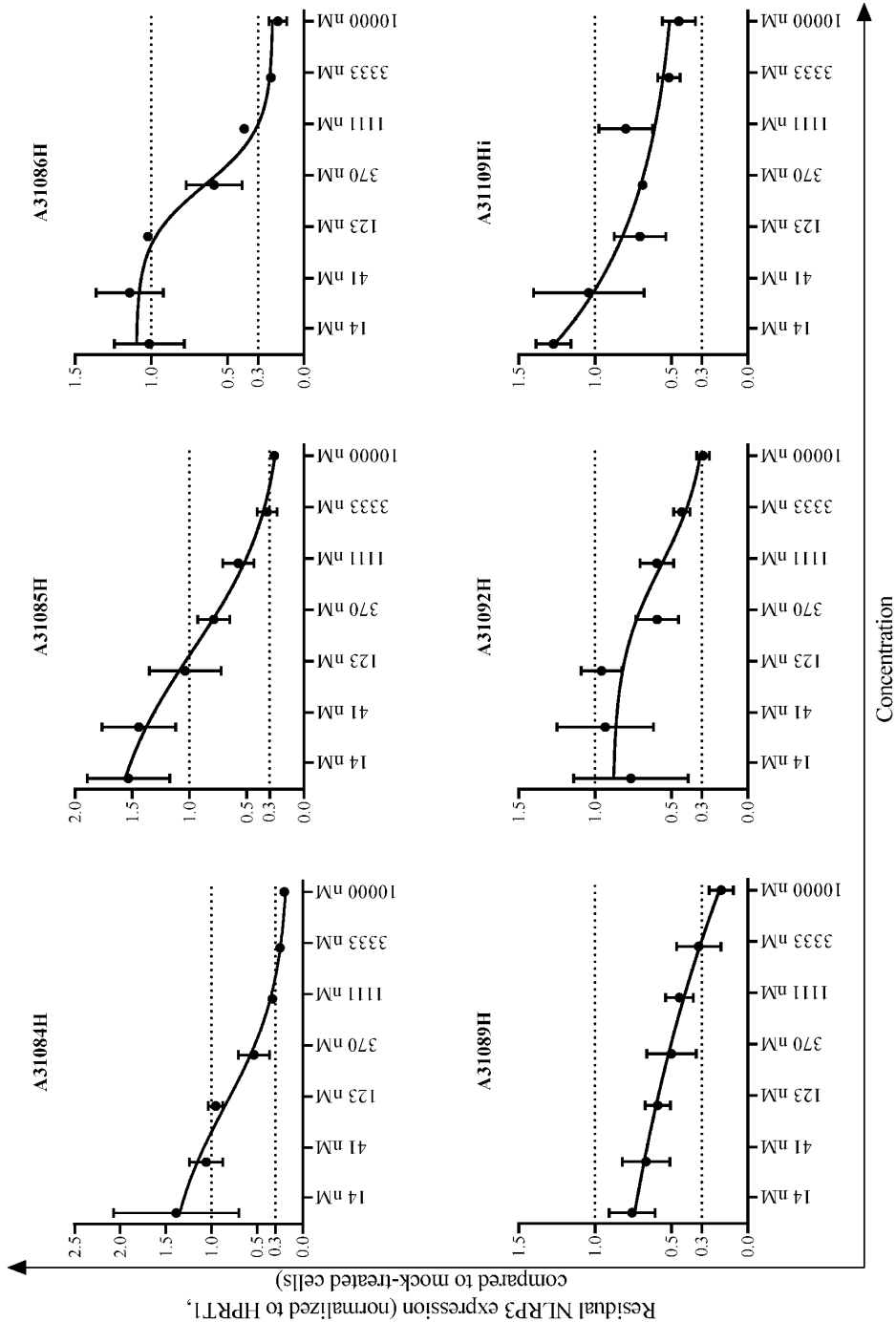


Fig. 7 continued): Concentration response curve of selected human NLRP3-specific ASOs in human PBMC-derived macrophages

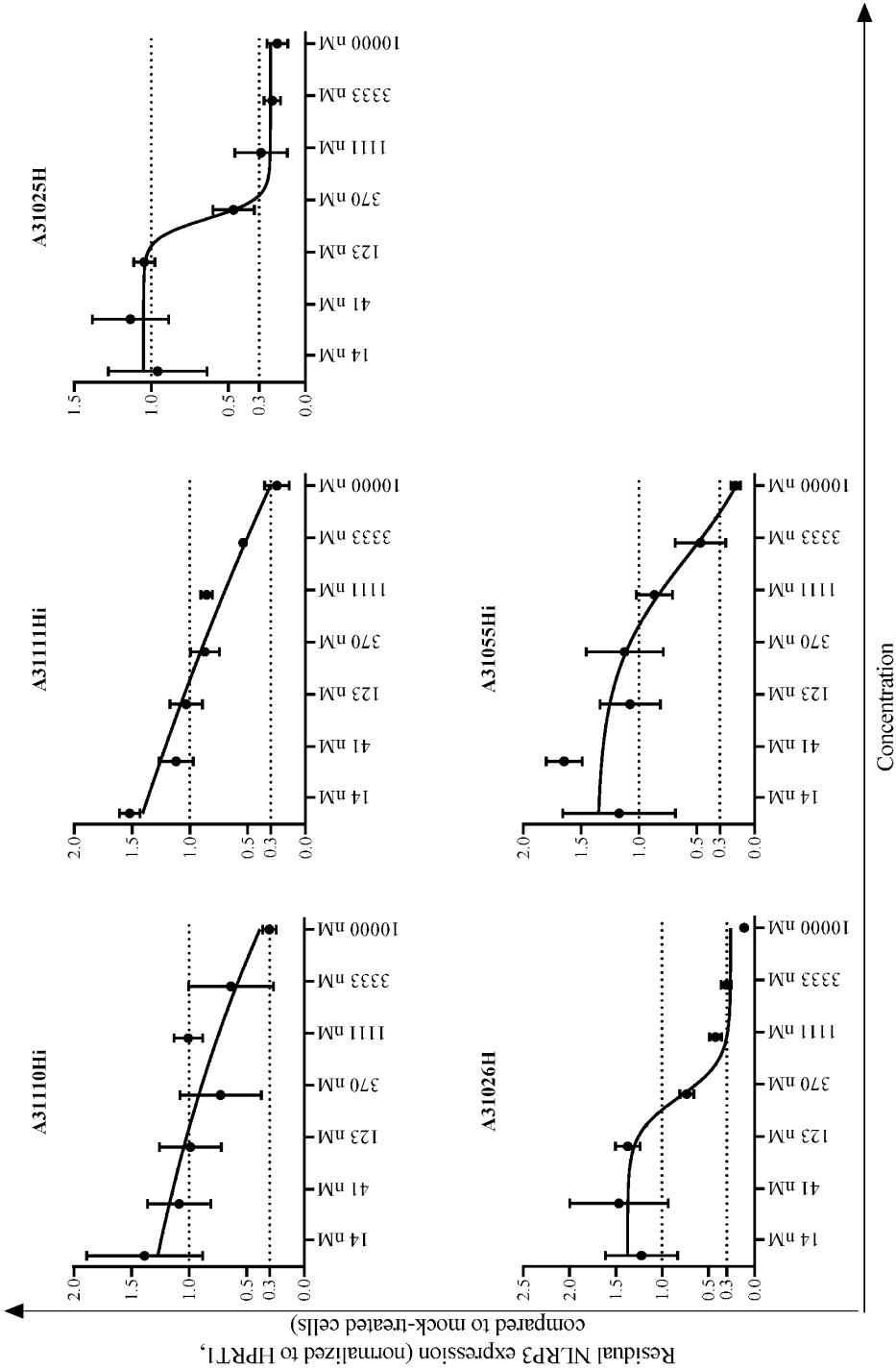


Fig. 8: Single concentration efficacy screen of human NLRP3-specific antisense oligonucleotides in THP-1-derived macrophages in a third screening round

Fig. 8)

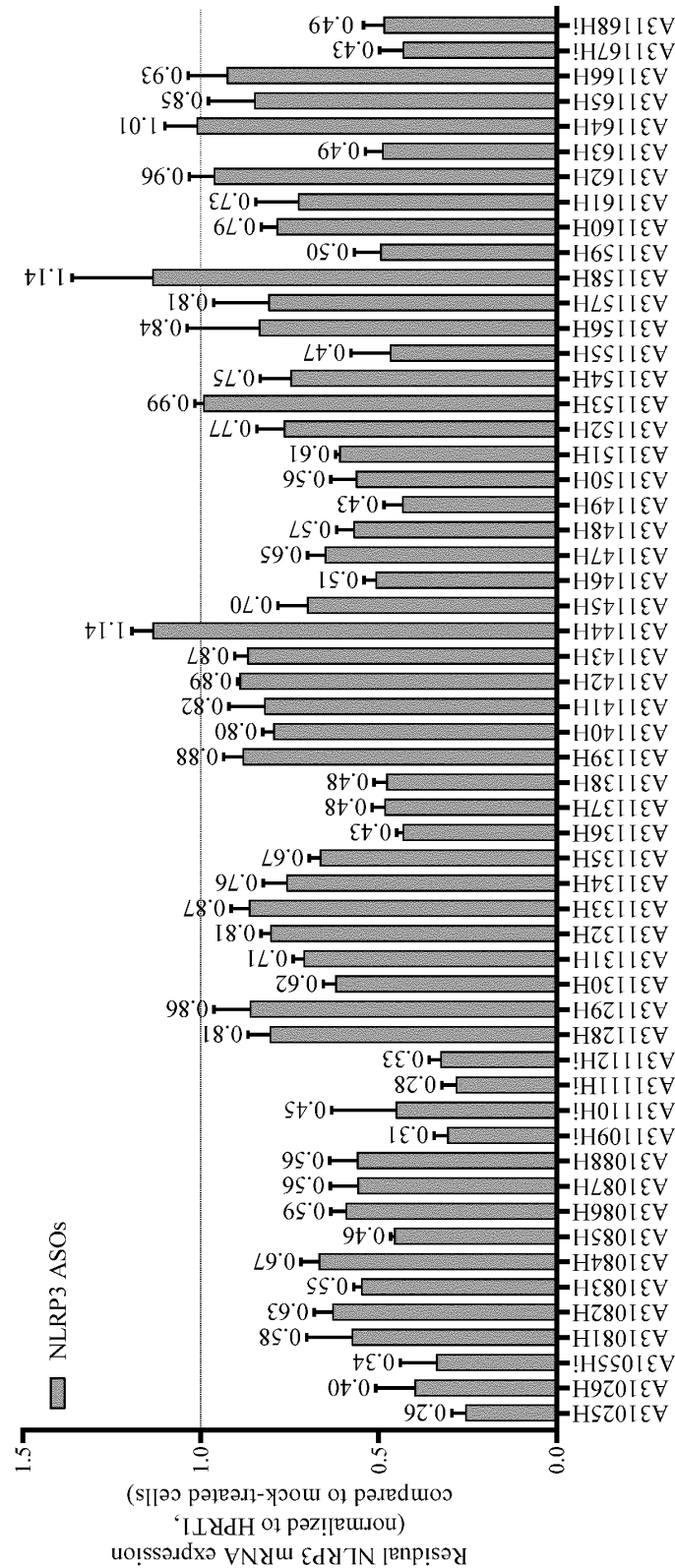


Fig. 8 continued)

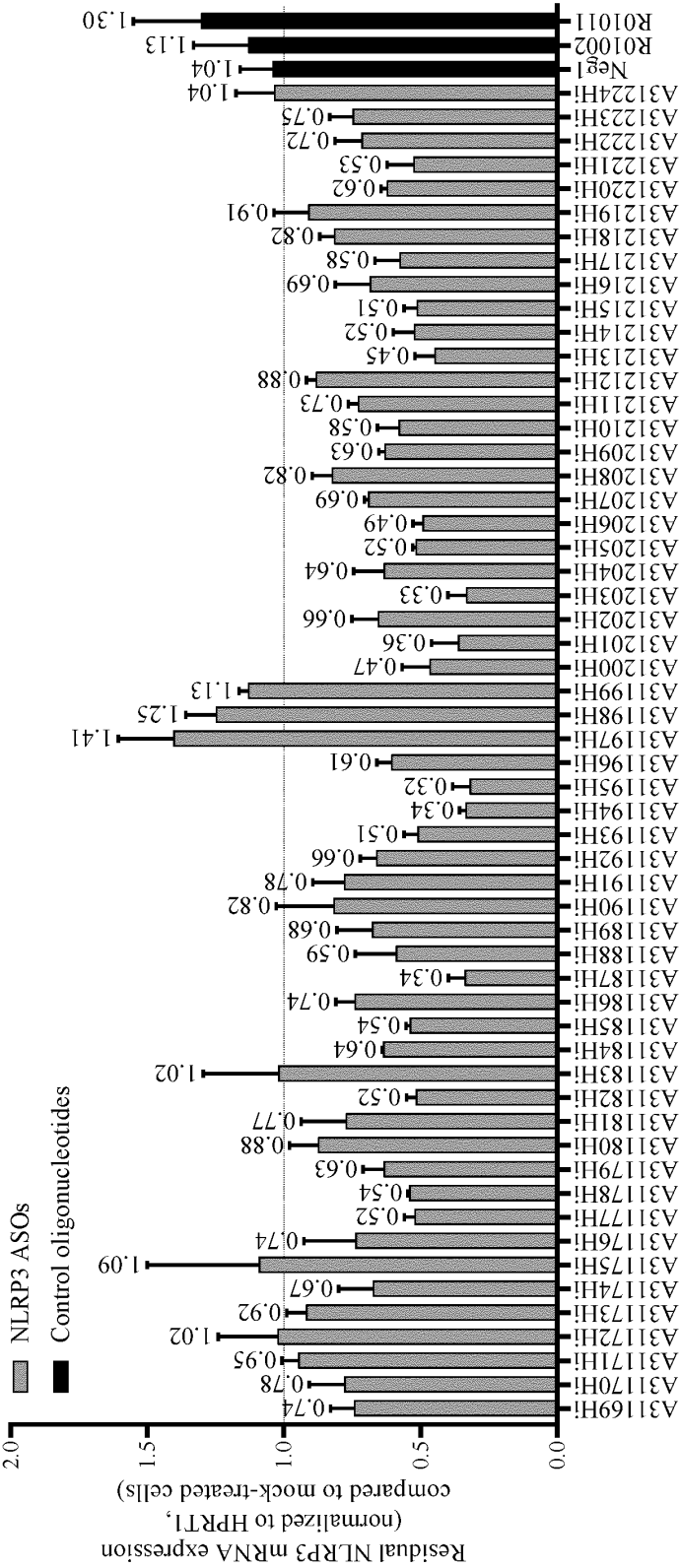


Fig. 9: Single concentration efficacy screen of human NLRP3-specific antisense oligonucleotides in human PBMC-derived macrophages in a third screening round

Fig. 9)

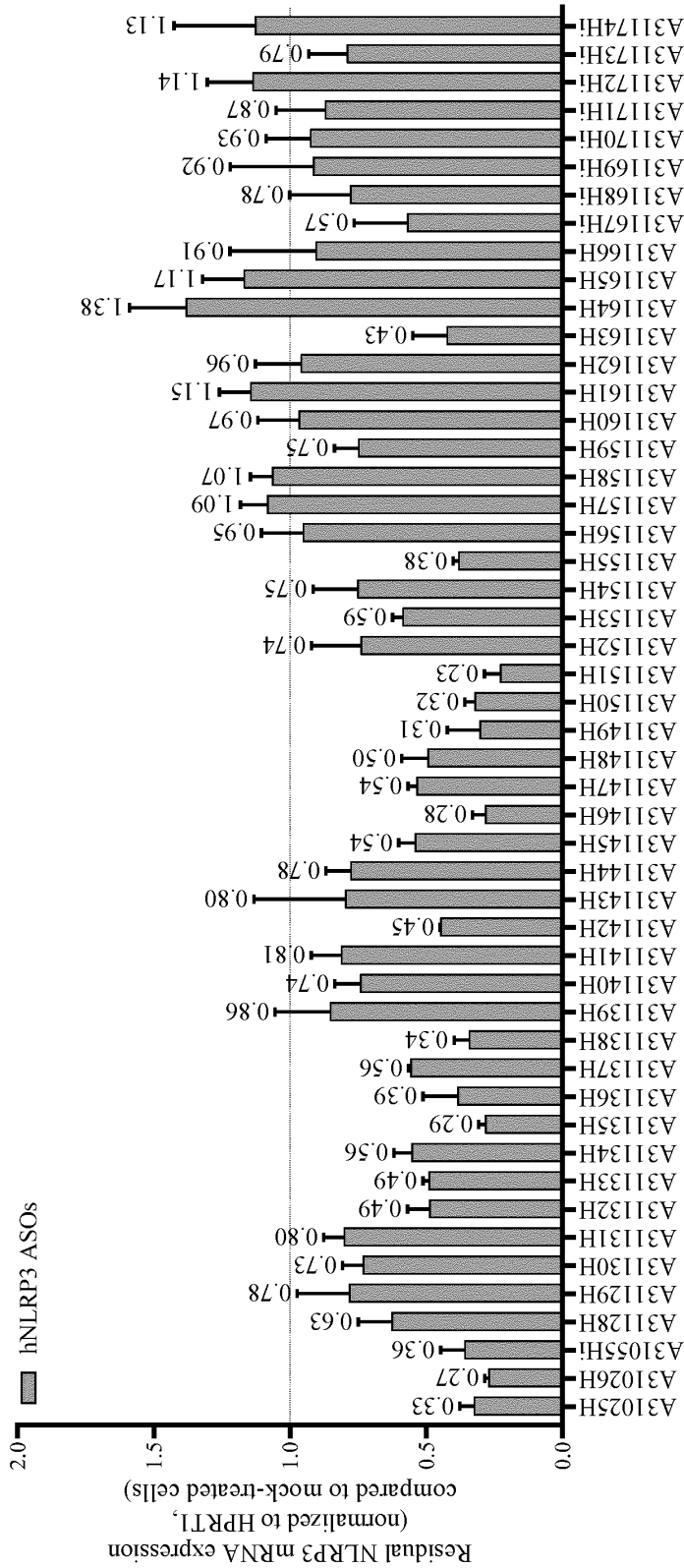


Fig. 9 continued)

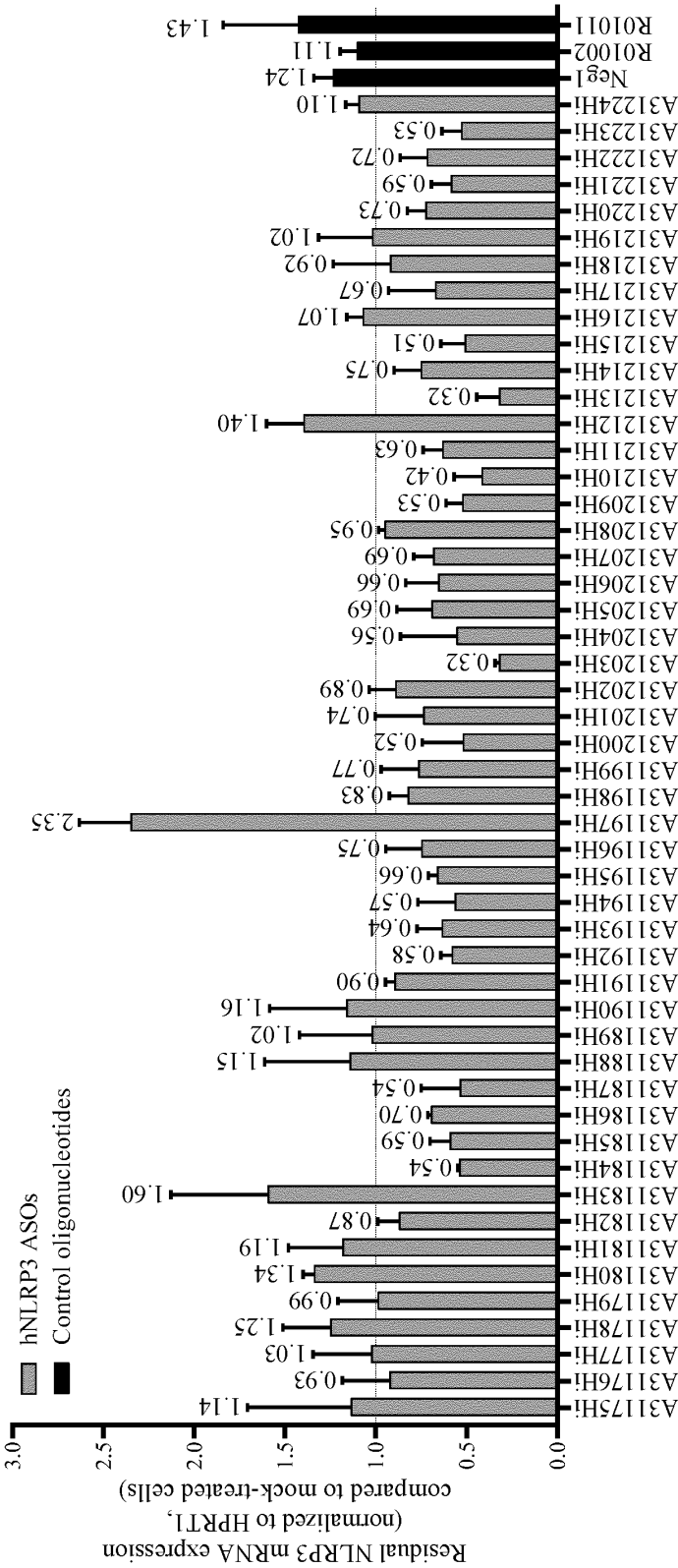


Fig. 10: Single concentration efficacy screen of human NLRP3-specific antisense oligonucleotides in THP-1-derived macrophages in a fourth screening round

Fig. 10)

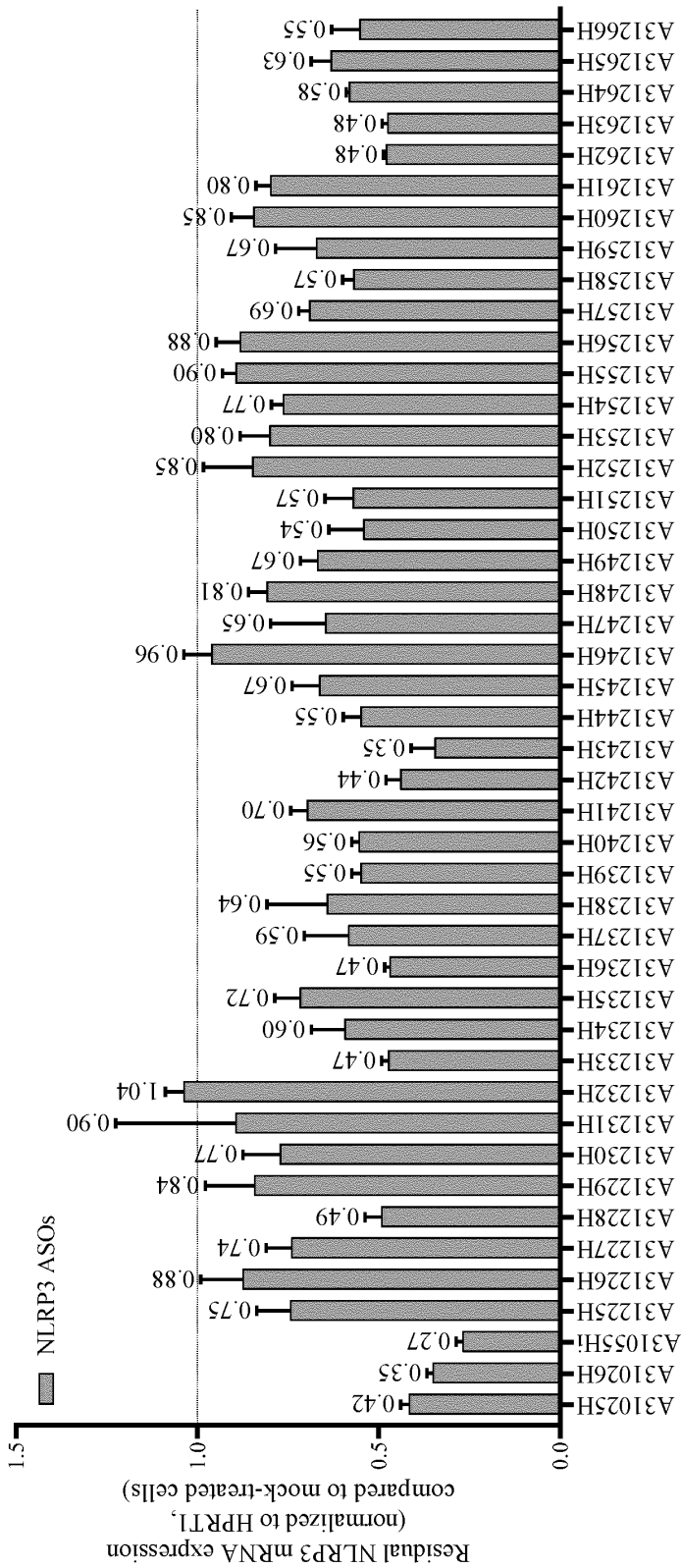


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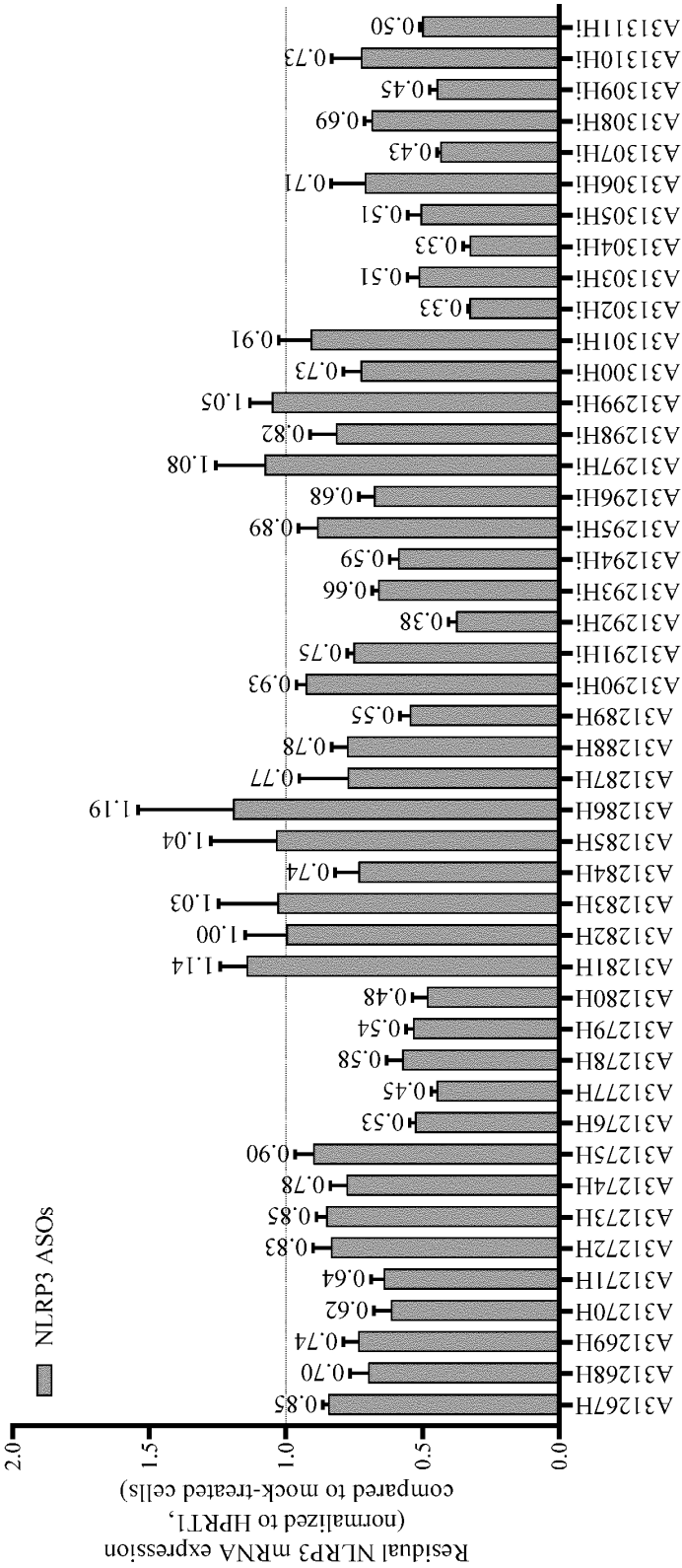


Fig. 10 continued)

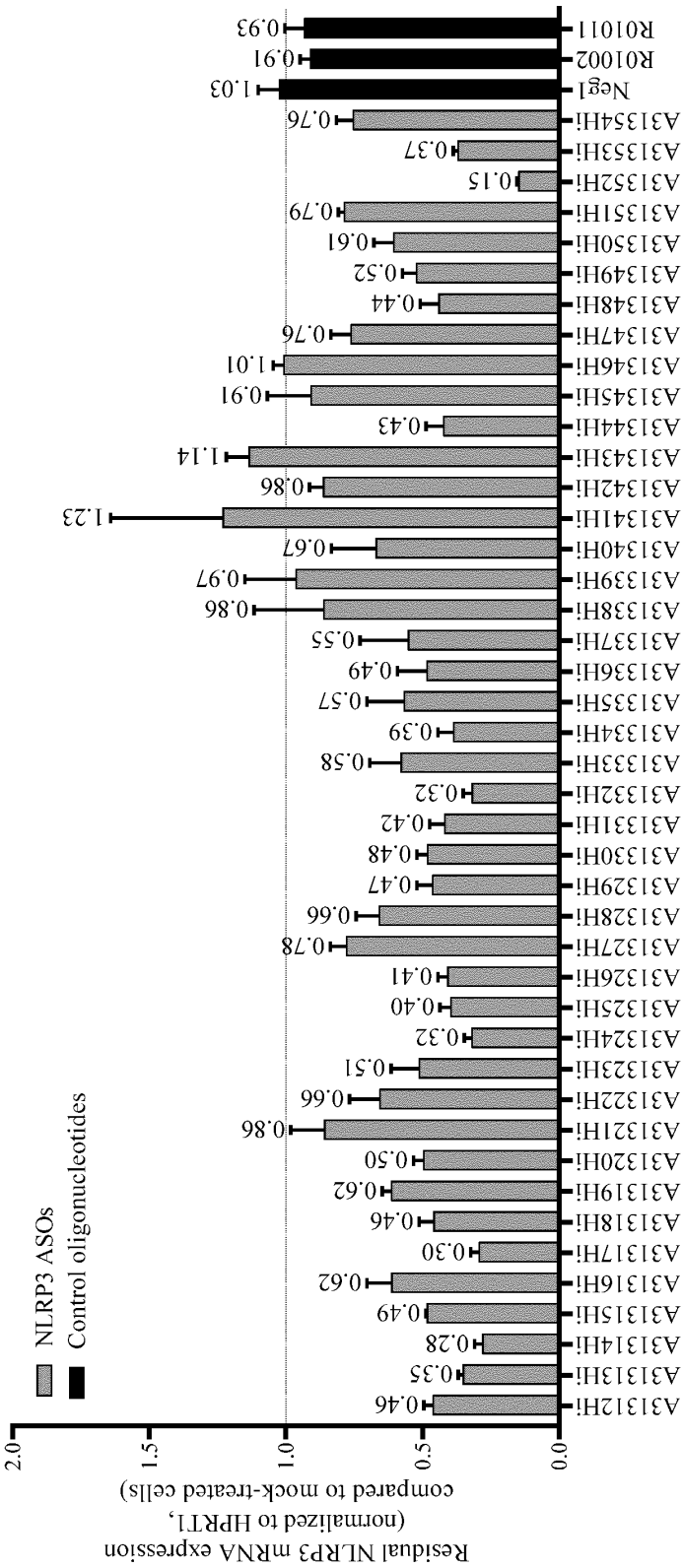


Fig. 11: Single concentration efficacy screen of human NLRP3-specific antisense oligonucleotides in PBMC-derived macrophages in a fourth screening round

Fig. 11)

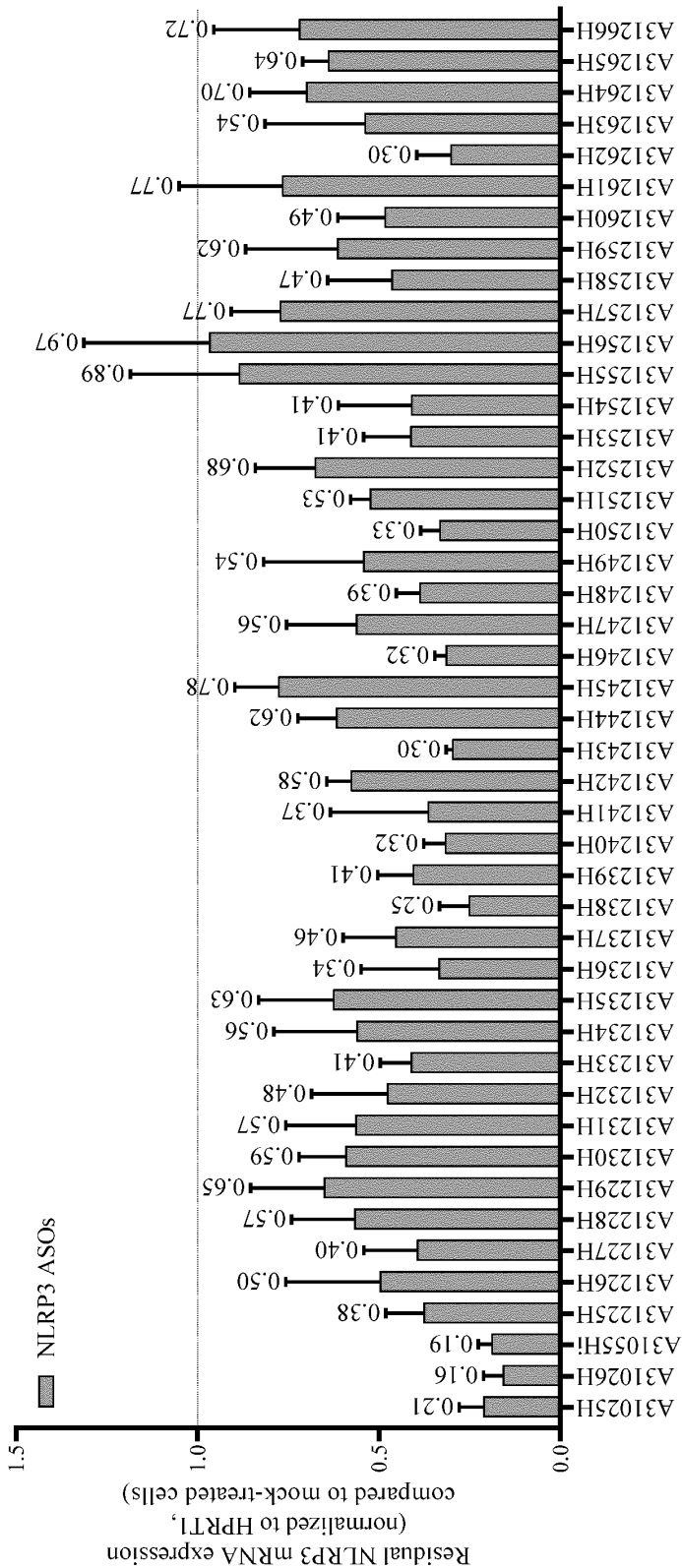


Fig. 11 continued)

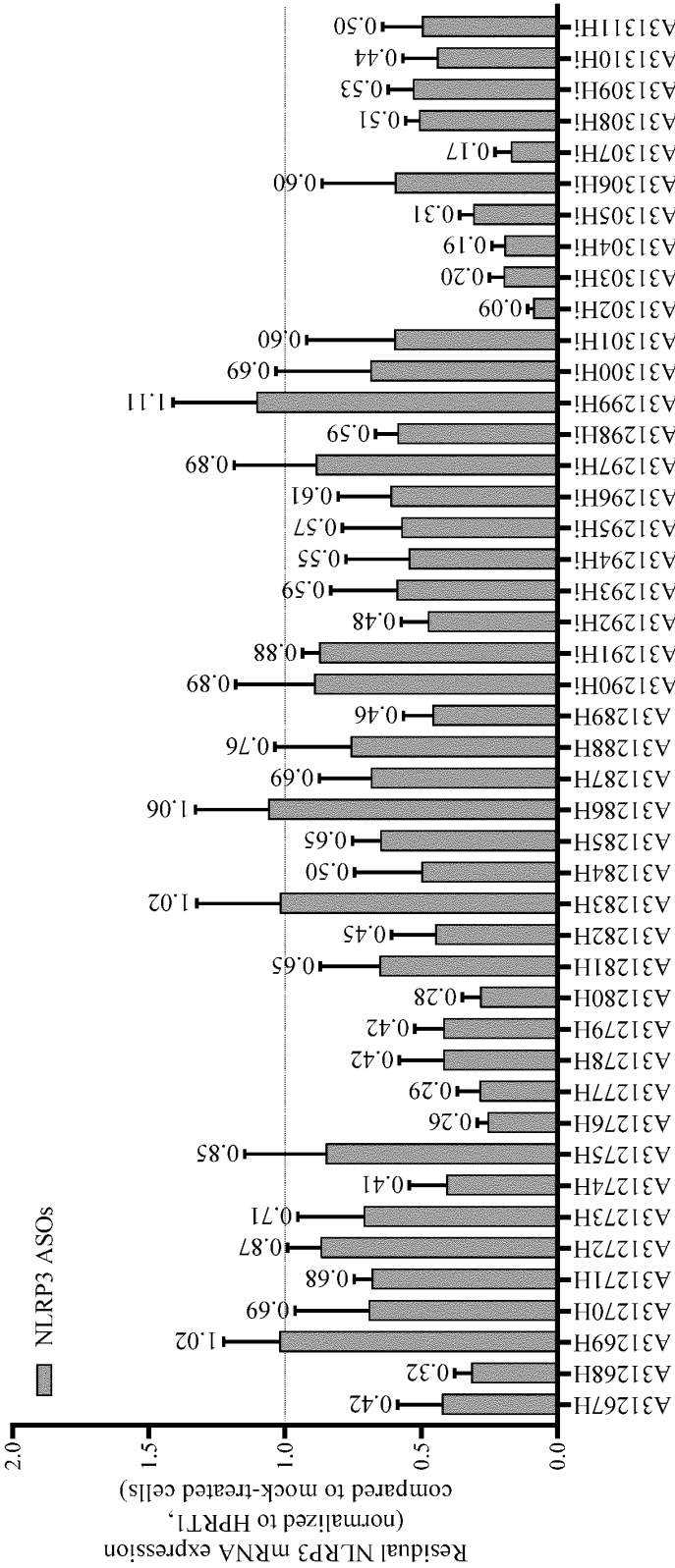


Fig.11 continued)

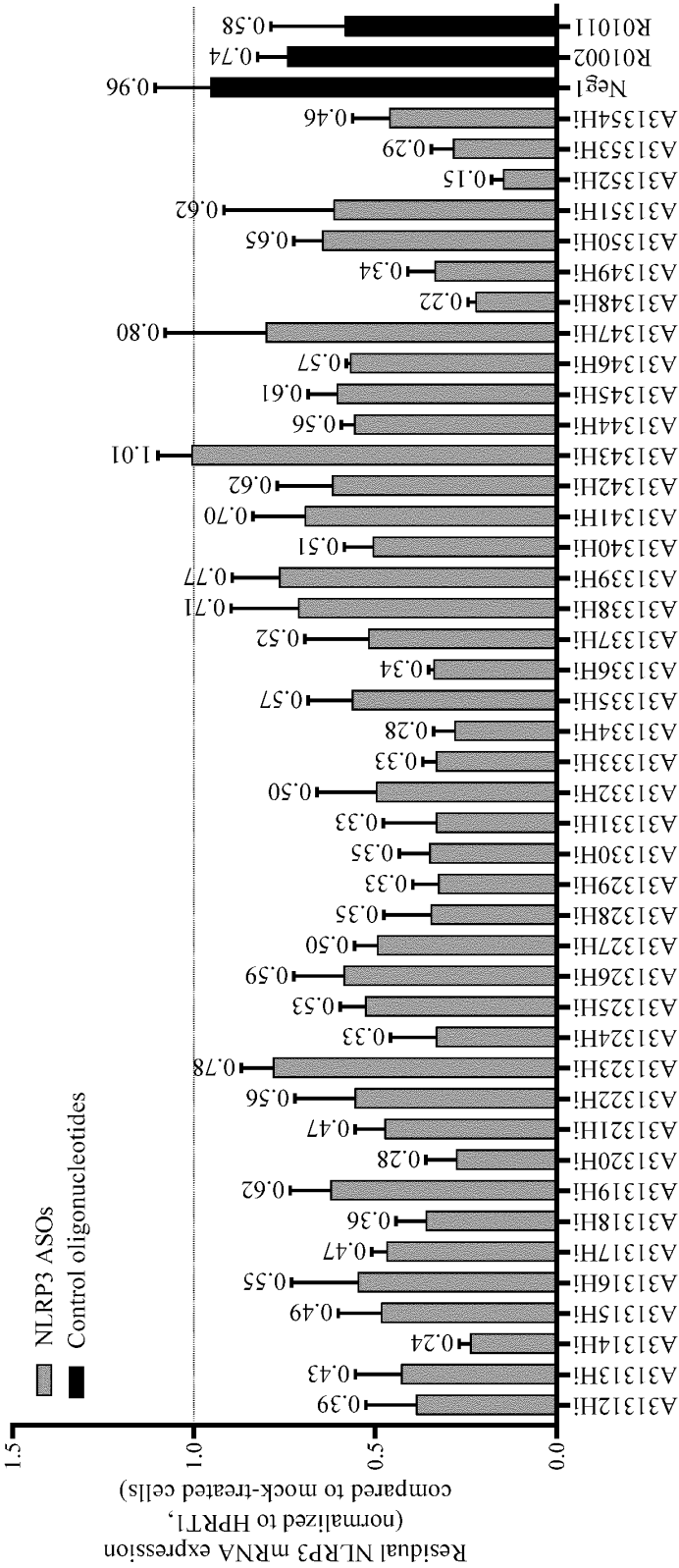


Fig. 12: Concentration response curve of selected human NLRP3-specific antisense oligonucleotides in THP-1-derived macrophages

Fig. 12)

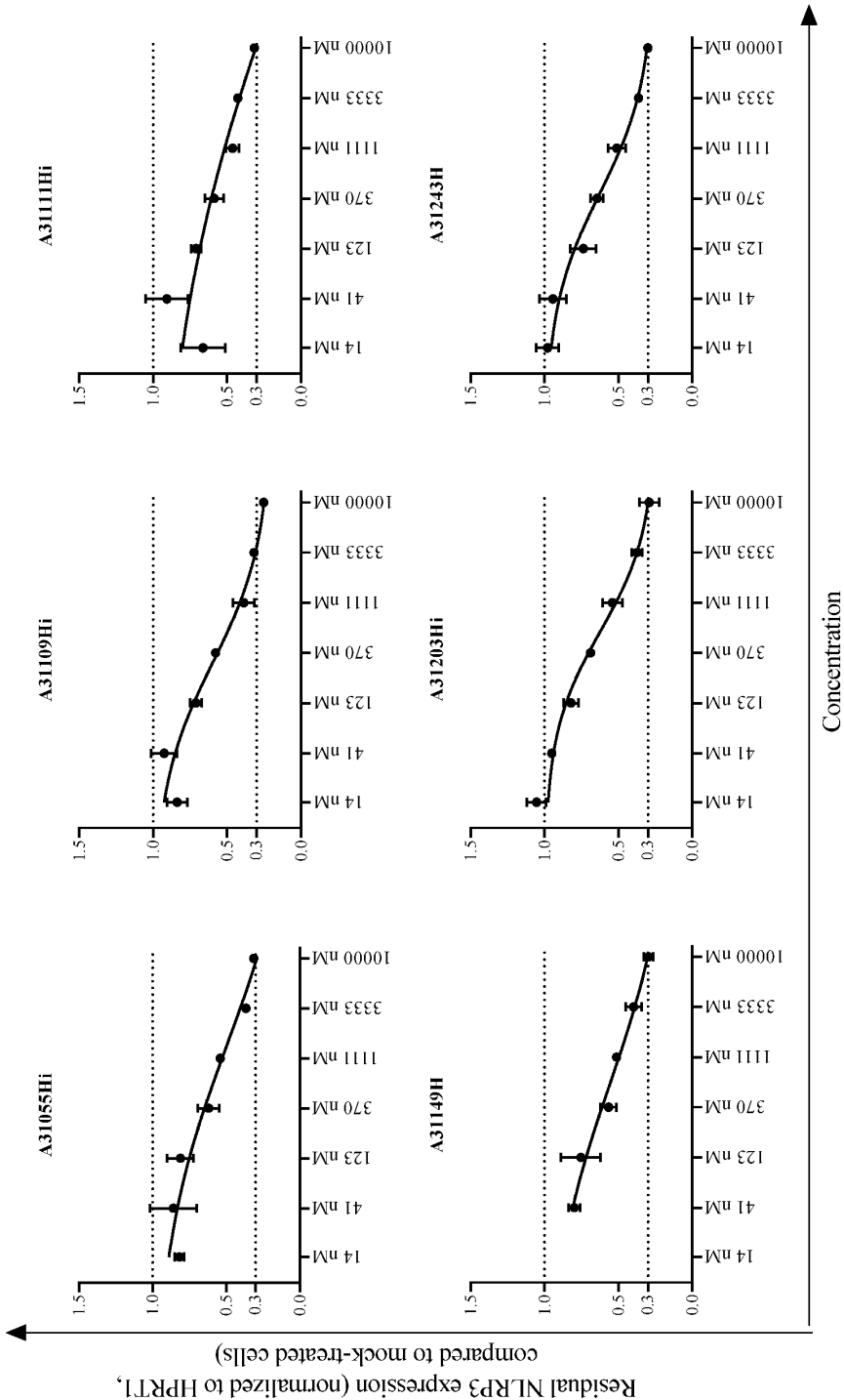
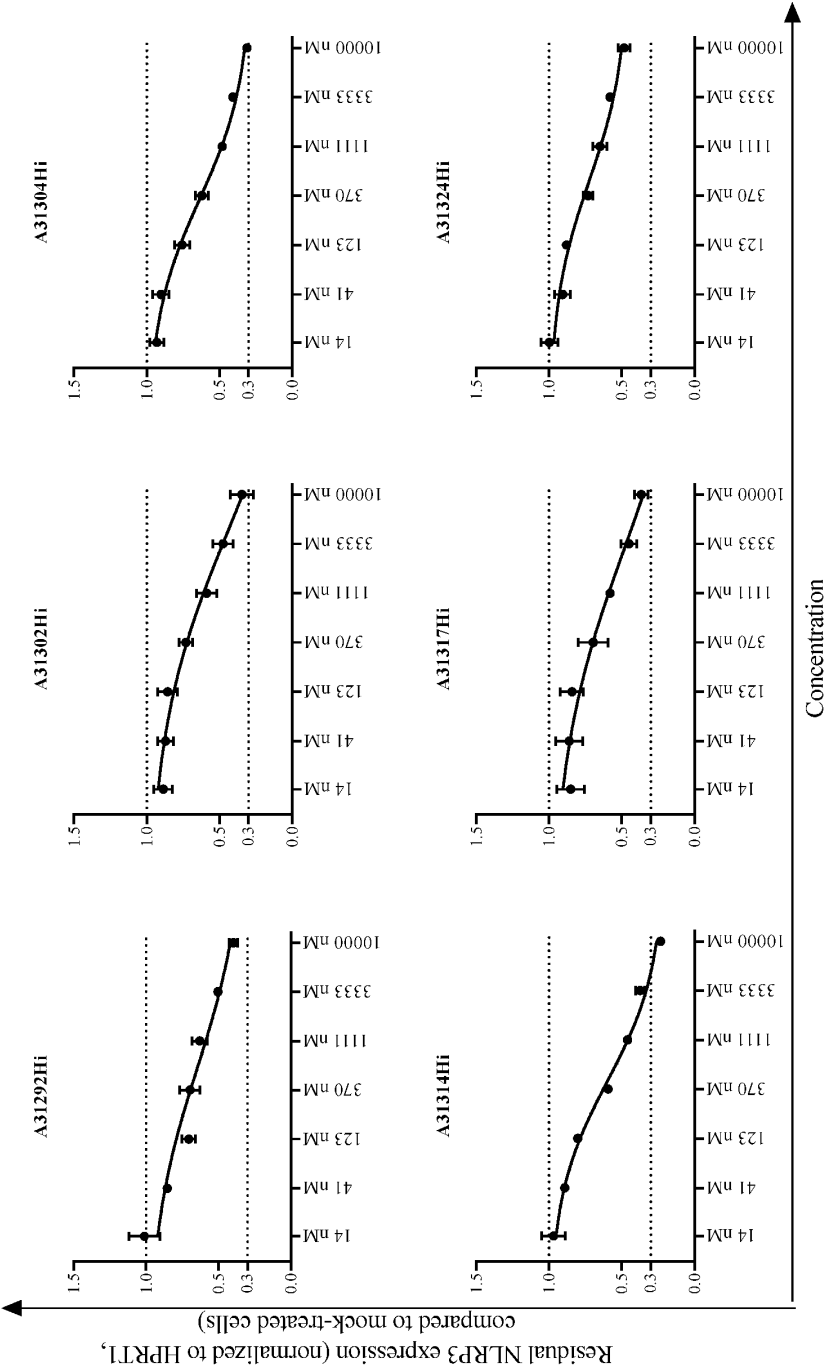


Fig. 12 continued)



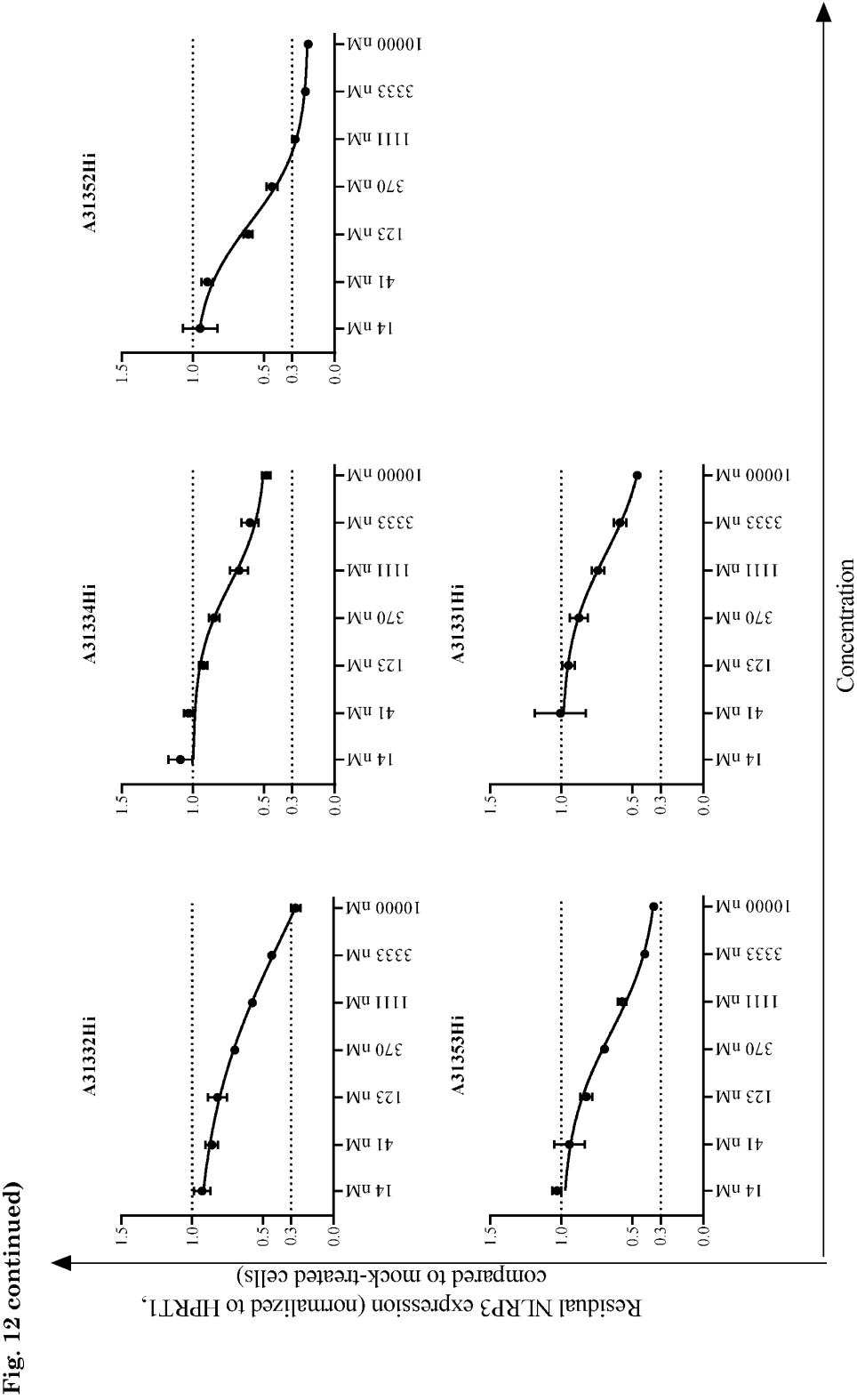


Fig. 13: Efficacy of selected human NLRP3-specific antisense oligonucleotides in human microglial HMC3 cells

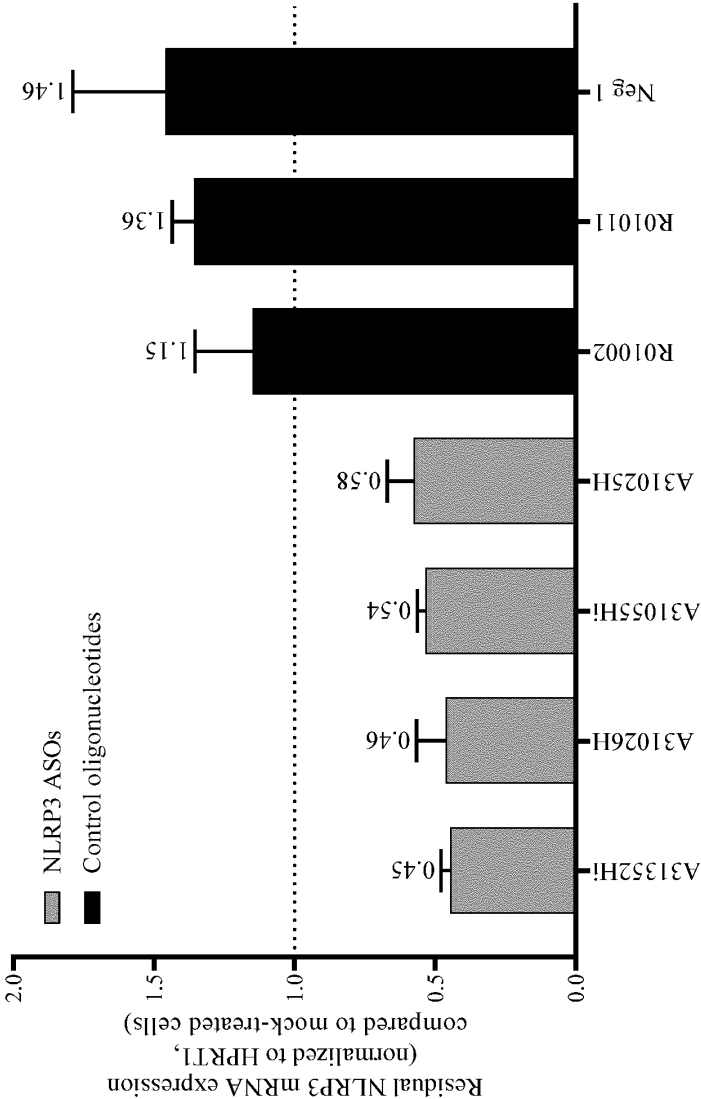


Fig 14: Single concentration screen of human NLRP3-specific antisense oligonucleotides in human THP-1-derived macrophages in a fifth screening round

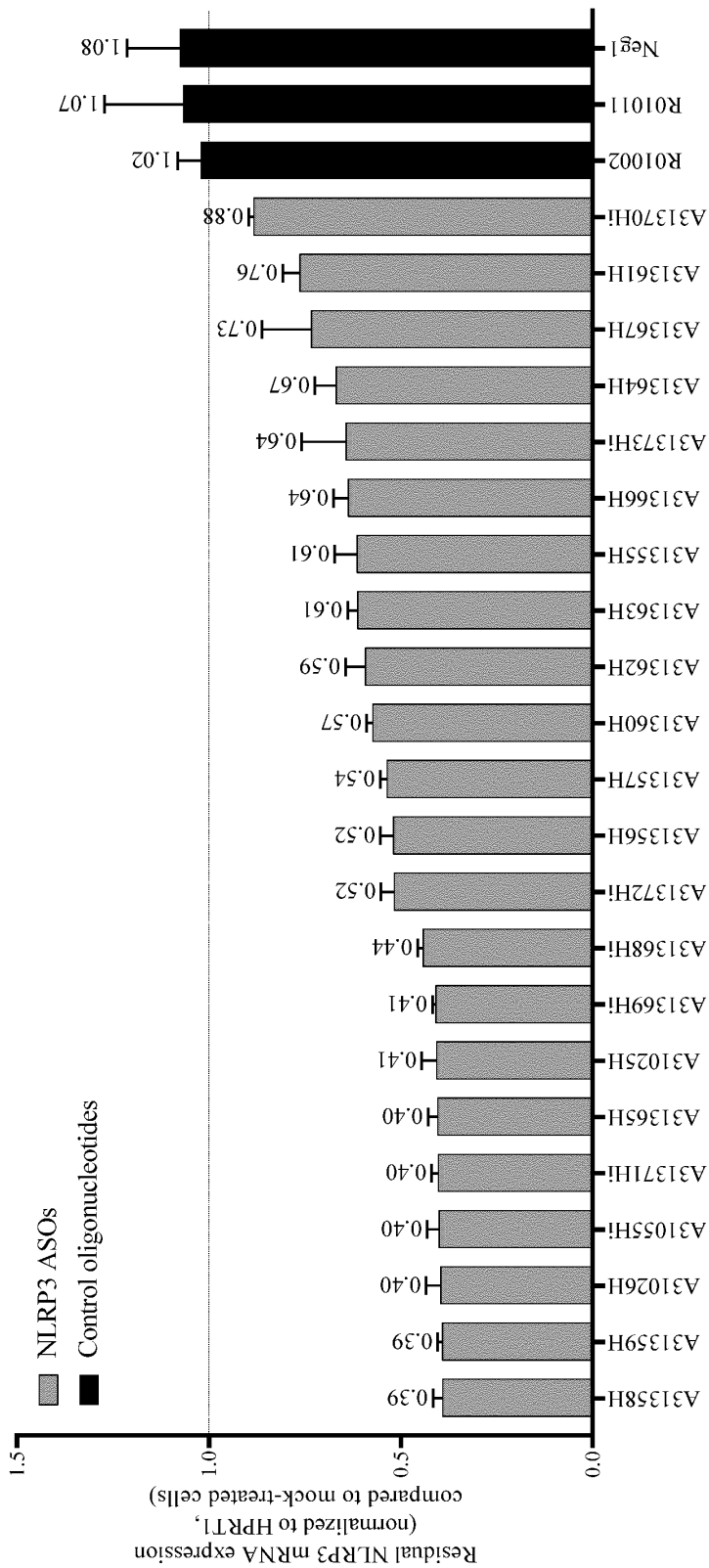


Fig 15: Single concentration screen of human NLRP3-specific antisense oligonucleotides in human PBMC-derived macrophages in a fifth screening round

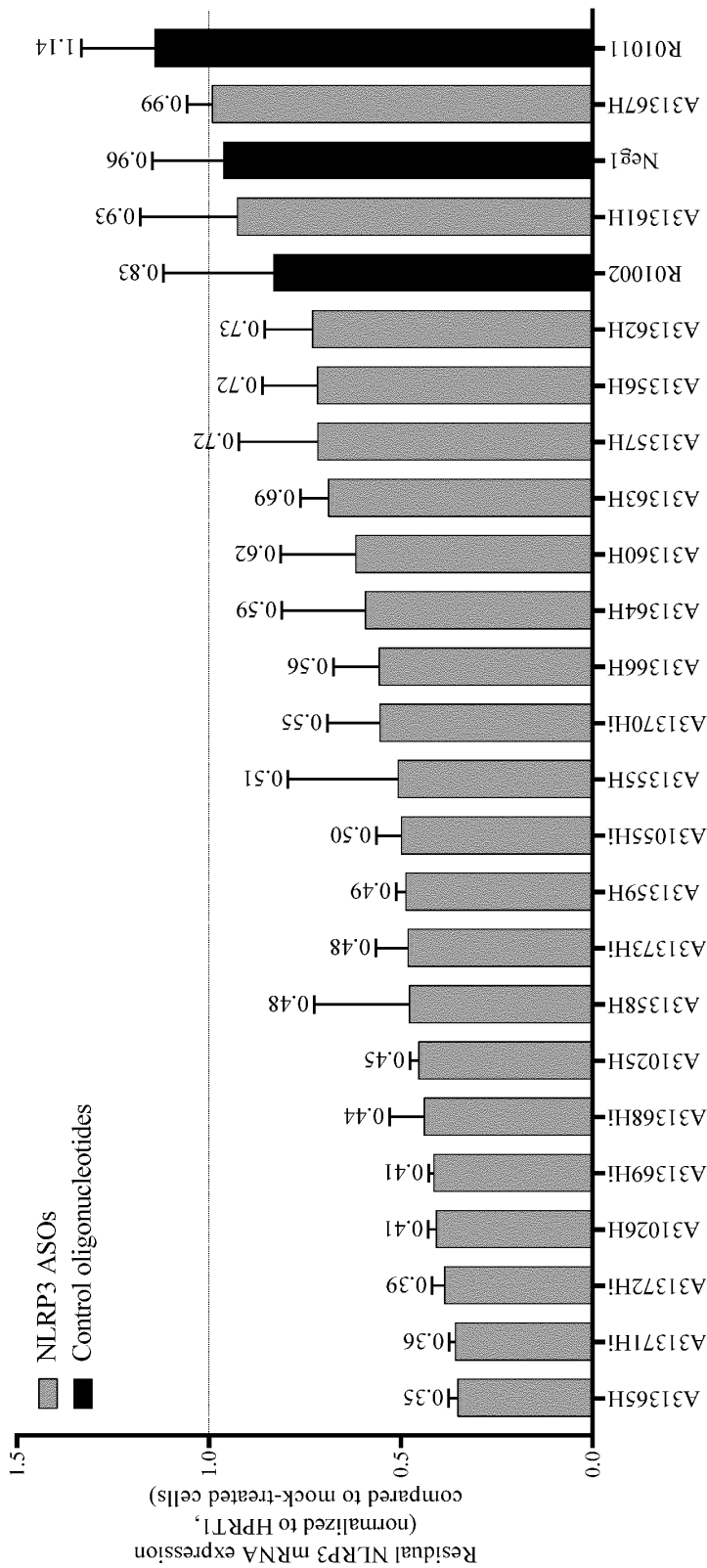
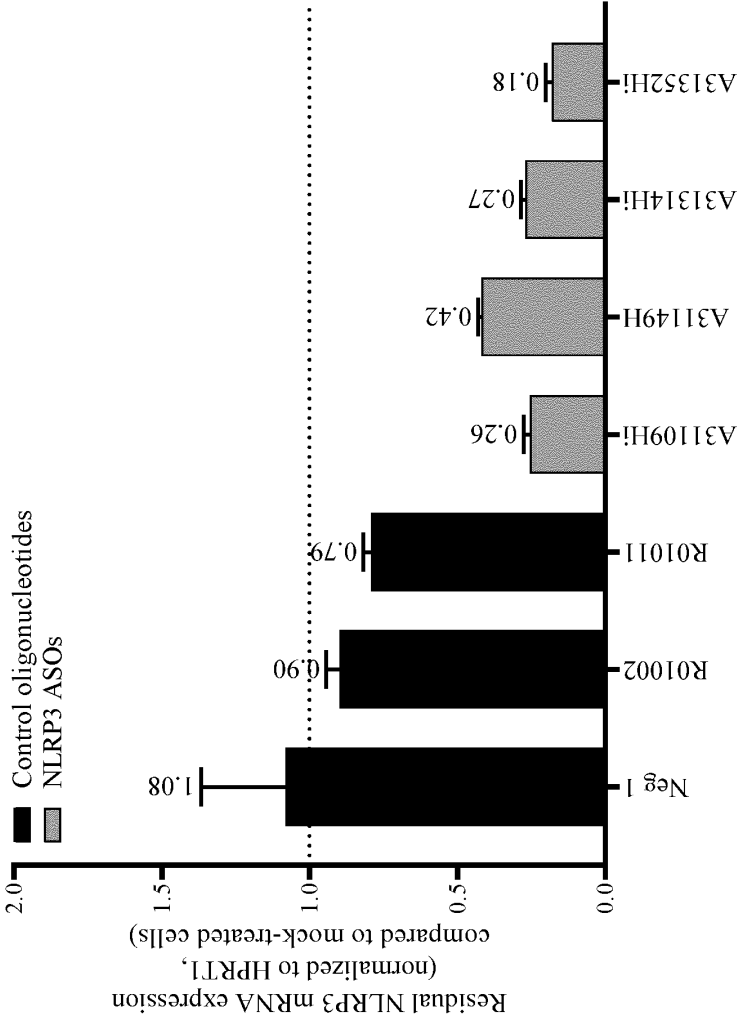
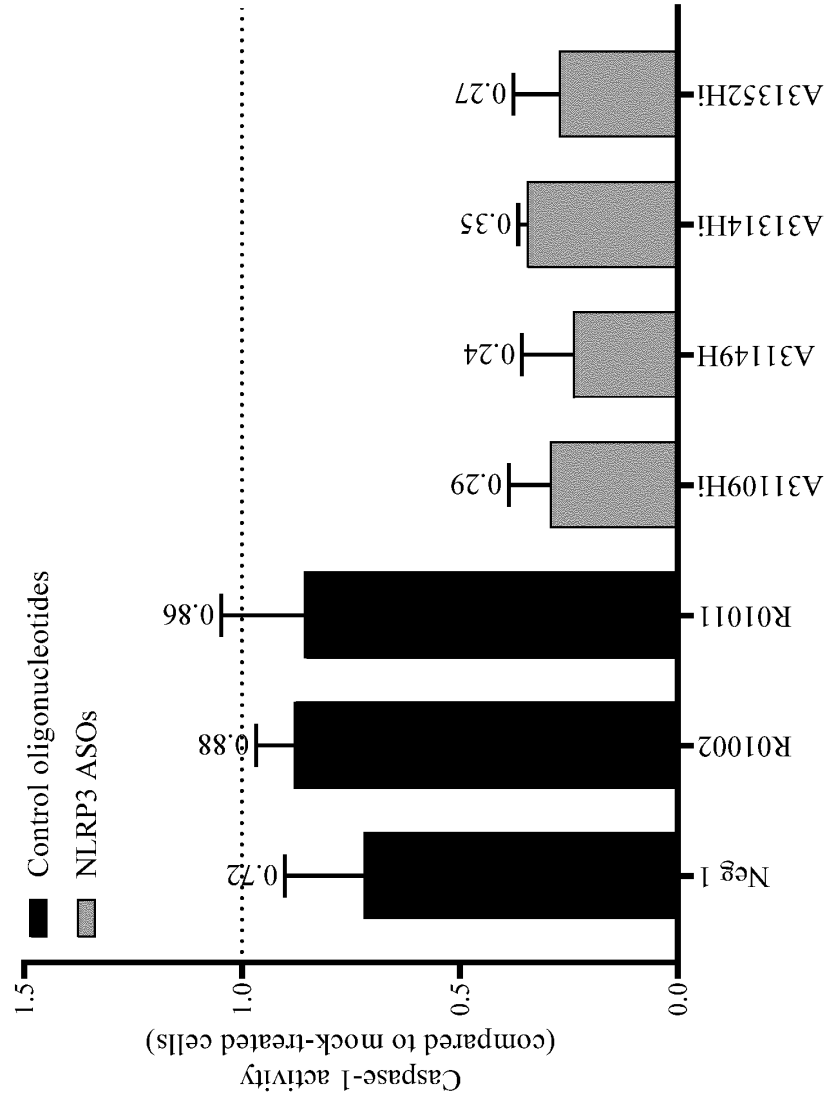


Fig 16A to 16C: Functional characterization of human NLRP3-specific ASOs in THP-1-derived macrophages

16A) Residual NLRP3 mRNA expression in ASO-treated THP-1 derived macrophages



16B) Caspase-1 activity assay in ASO-treated THP-1 derived macrophages



16C) IL-1 β protein expression of pro-IL-1 β and mature- IL-1 β in cell lysates and cell culture supernatants of ASO-treated THP-1-derived macrophages as analyzed by Western Blot

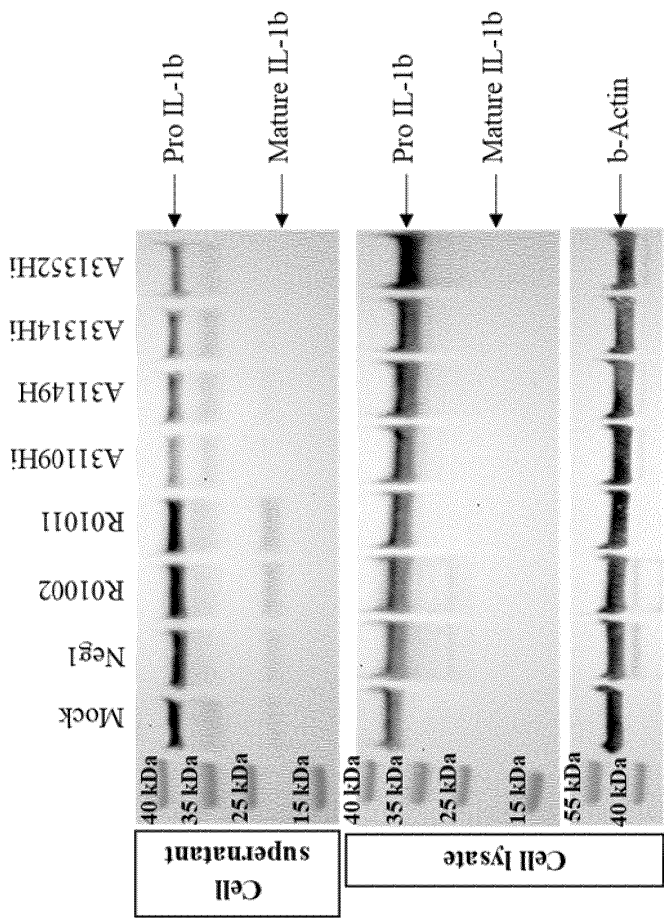


Fig. 17A and 17B: Single concentration efficacy screen for mouse NLRP3-specific antisense oligonucleotides in 4T1 cells

Fig. 17A) NLRP3 mRNA expression in ASO-treated 4T1 cells compared to mock-treated cells

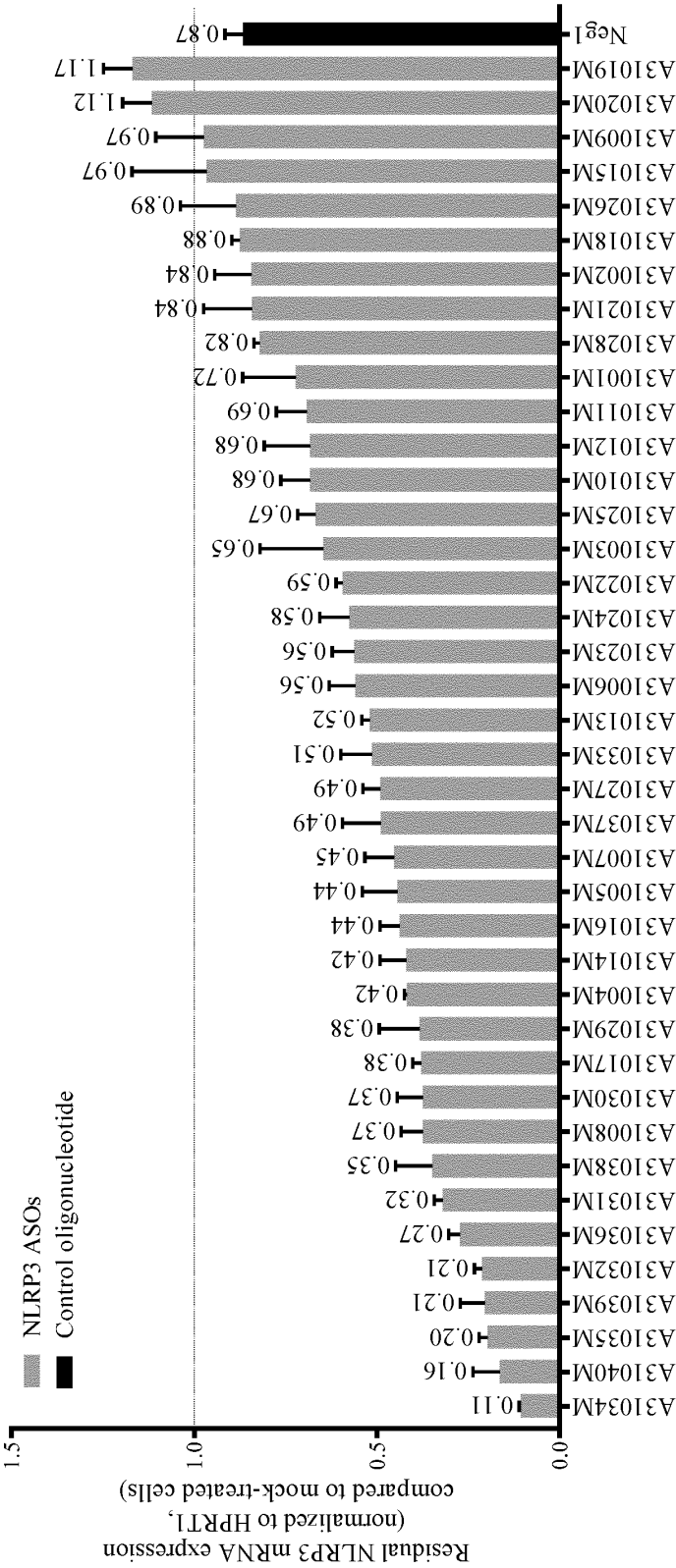


Fig. 17B) Cell viability of 4T1 cells after three days ASO treatment

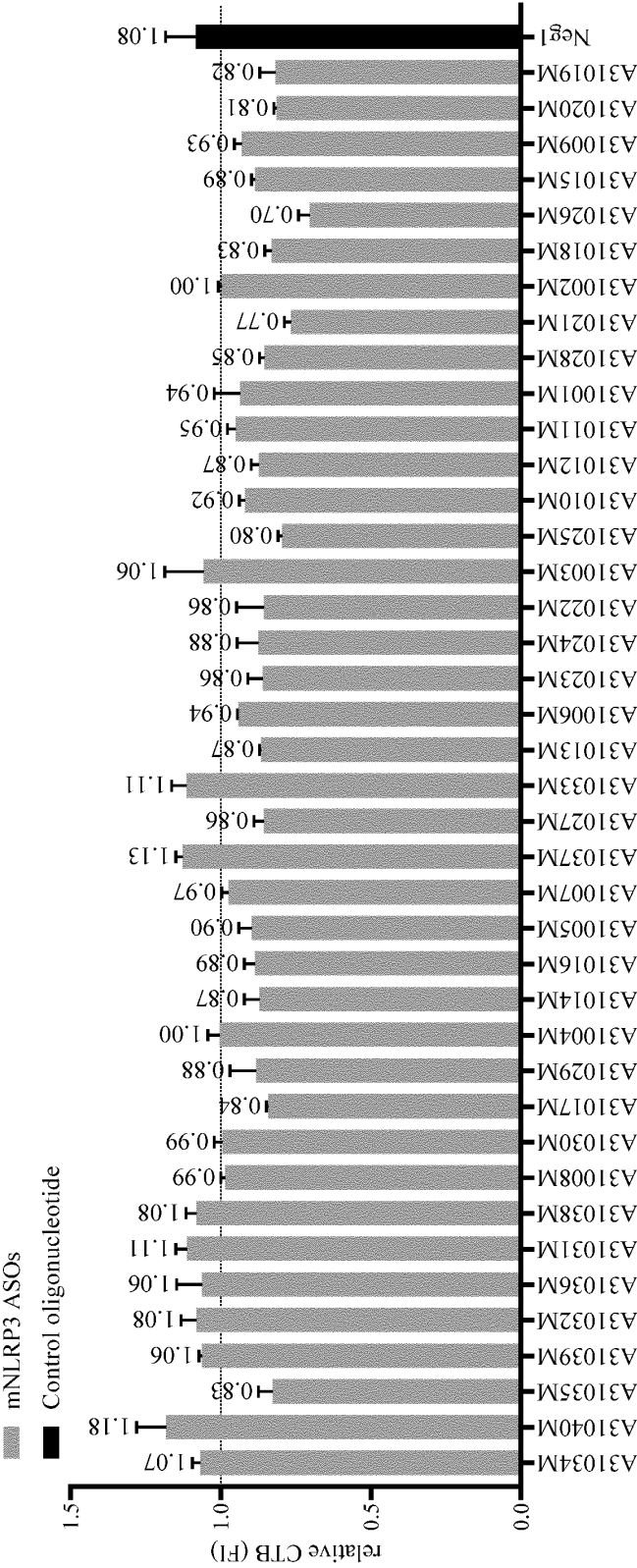


Fig. 18: Single concentration efficacy screen for mouse NLRP3-specific antisense oligonucleotides in Raw246.7 cells – first screening

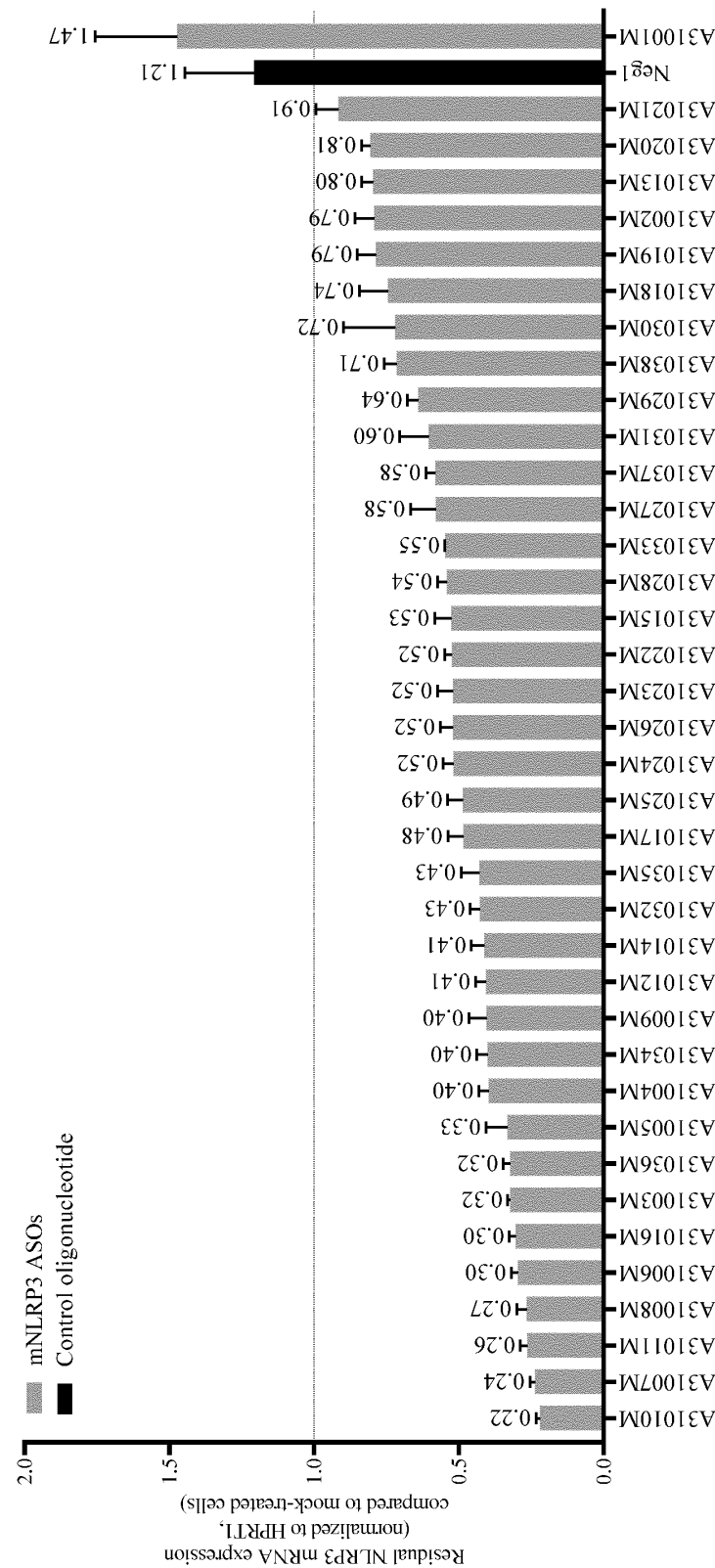


Fig. 19: Single dose efficacy screen for mouse NLRP3-specific antisense oligonucleotides in Raw246.7 cells – second screening

Fig. 19A) NLRP3 mRNA expression in ASO-treated Raw246.7 cells compared to mock-treated cells

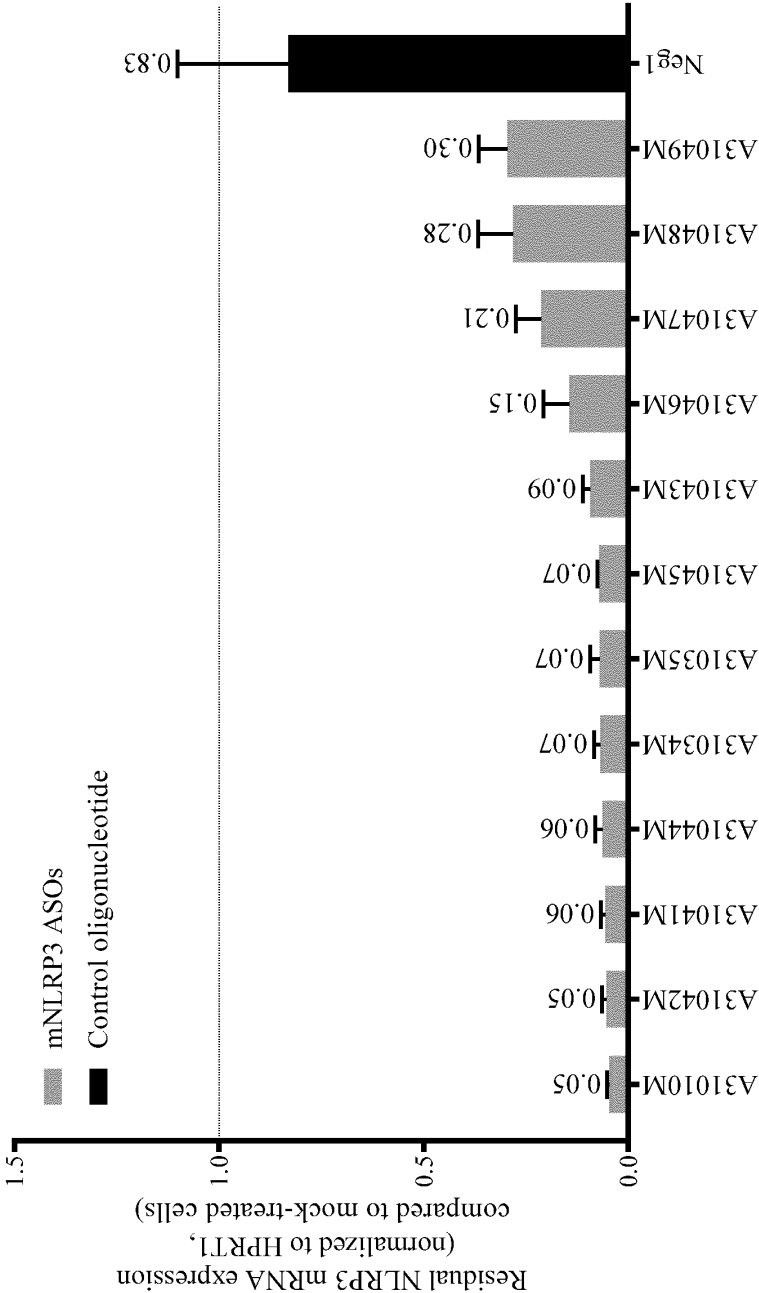


Fig. 19B)

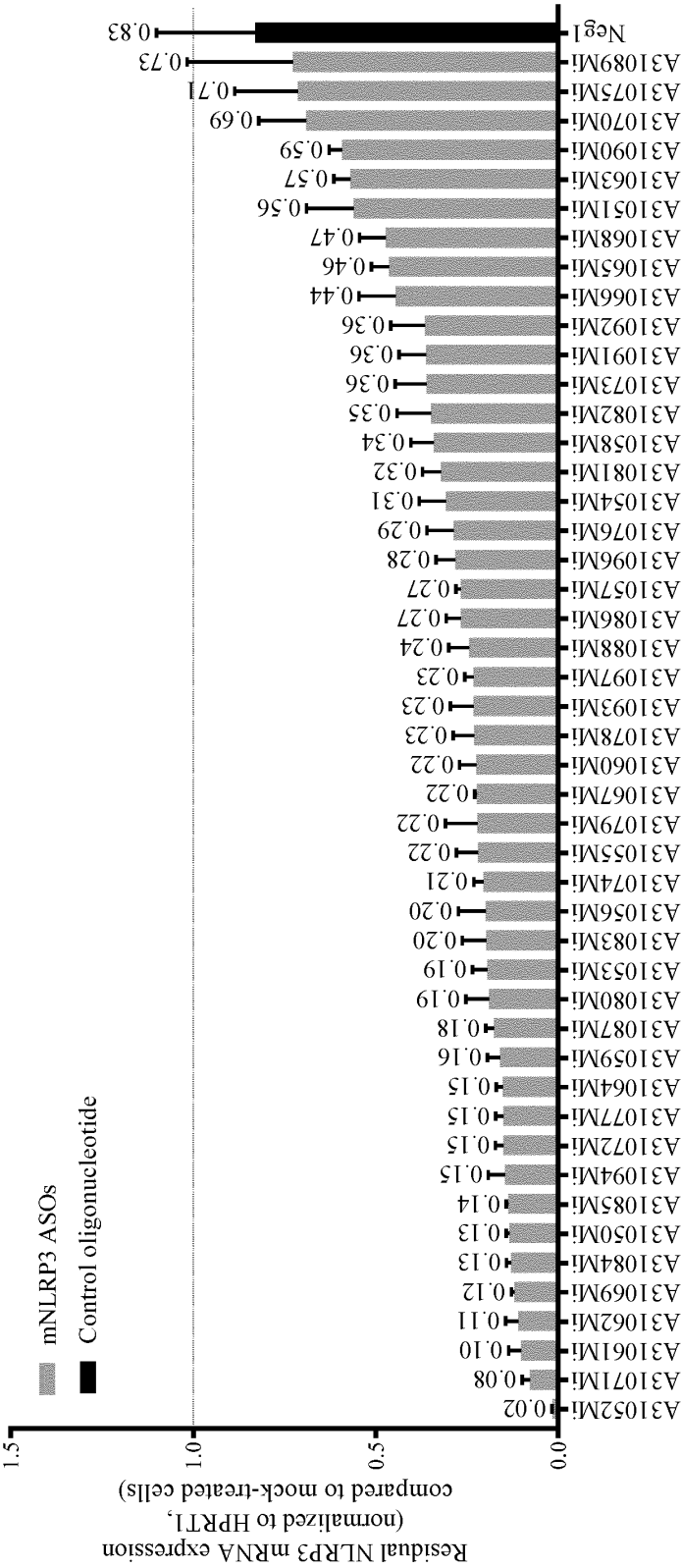


Fig. 20: Single concentration efficacy screen for mouse NLRP3-specific antisense oligonucleotides in 4T1 cells – second screening

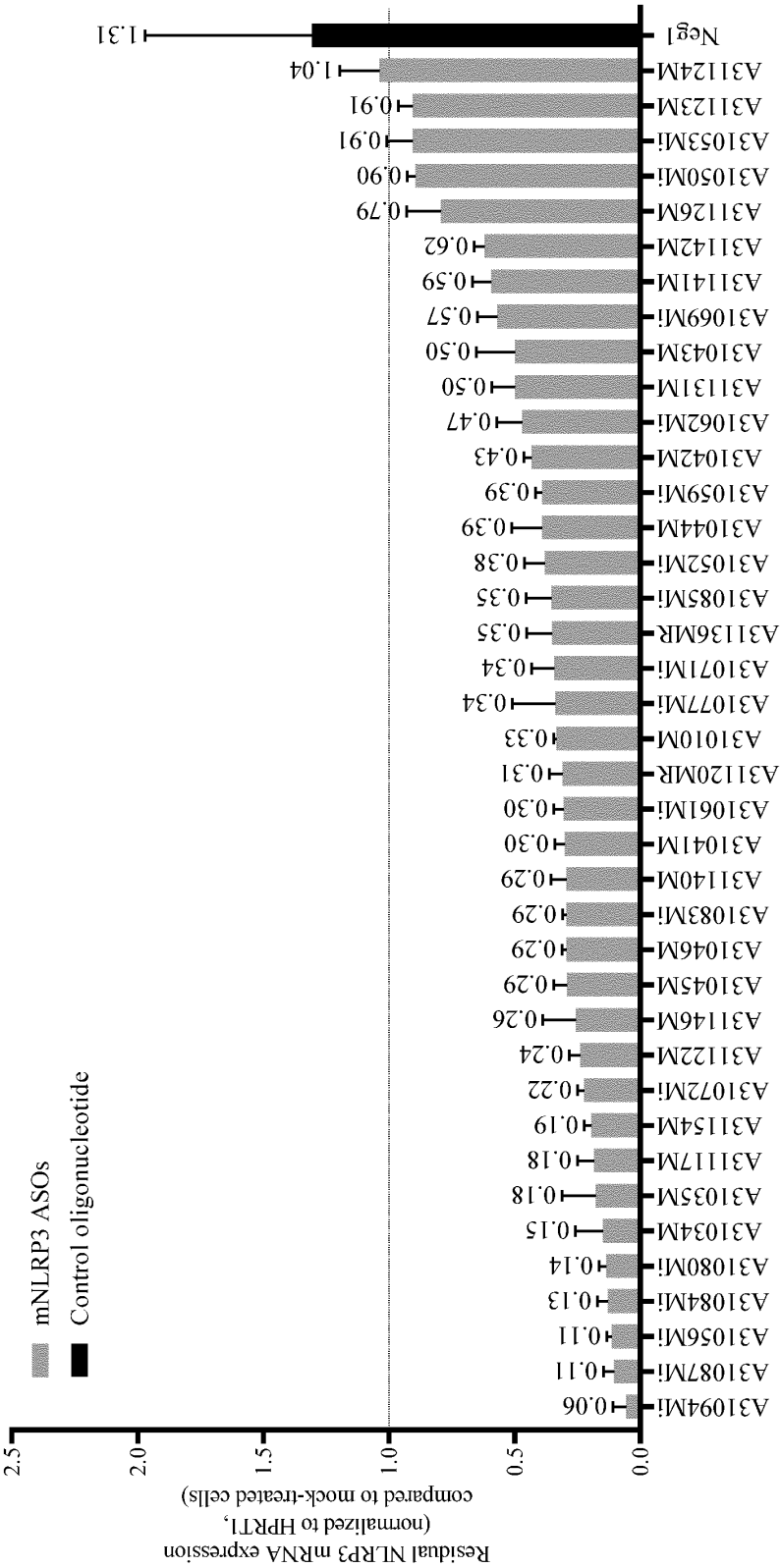


Fig. 21: Concentration response curve of selected mouse NLRP3-specific antisense oligonucleotides in Raw246.7 cells

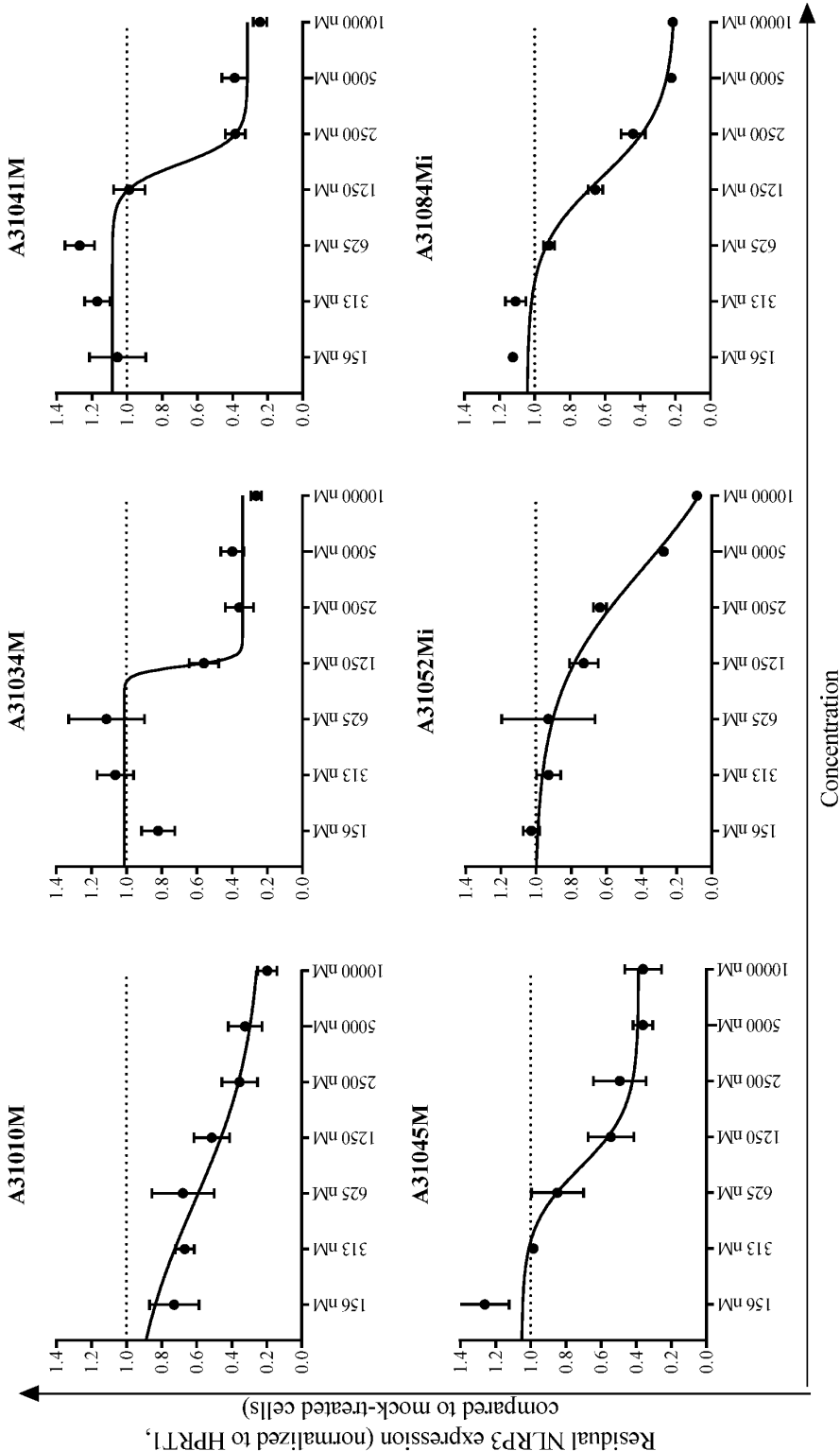


Fig. 21 continued)

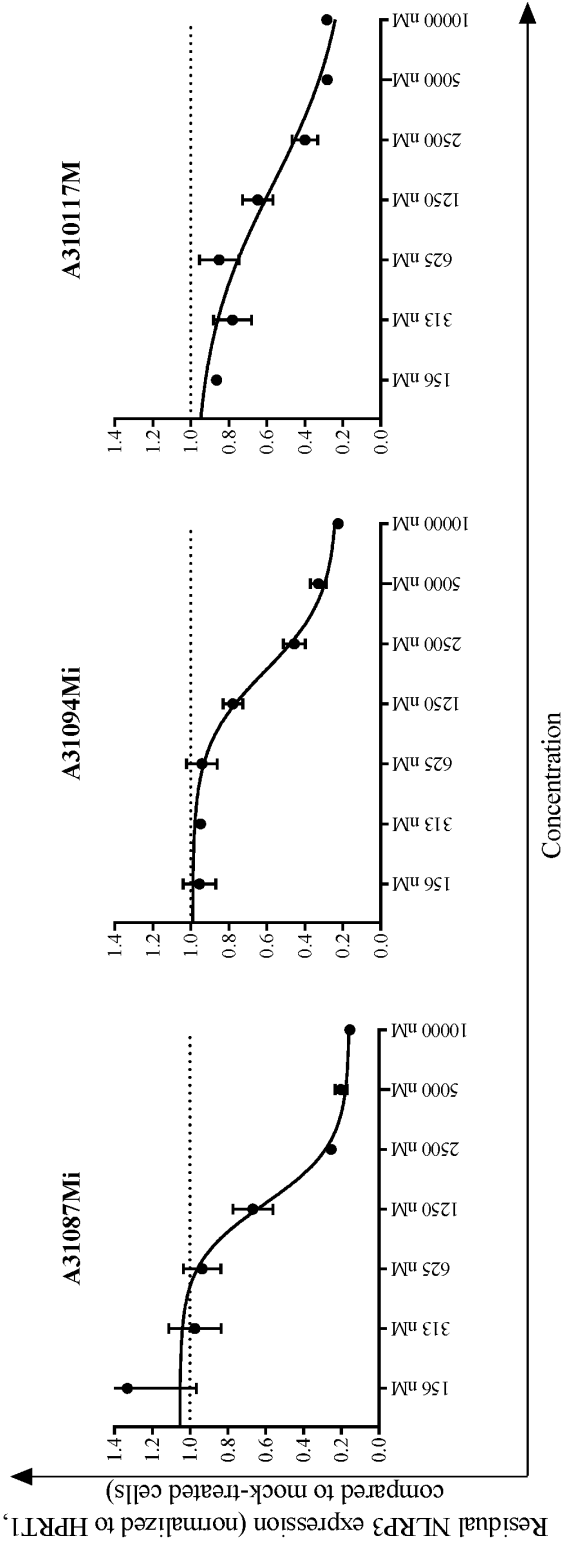


Fig. 22 A and 22 B: Mouse NLRP3-specific antisense oligonucleotide prevents cleavage of pro-IL-1 β in mouse bone marrow derived macrophages (BMDM)

Fig. 22 A) Residual NLRP3 mRNA expression in ASO-treated BMDM

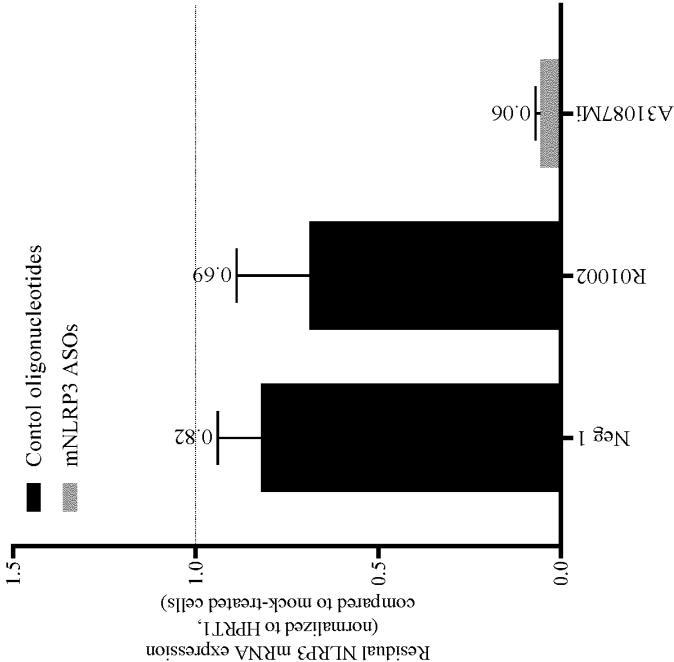


Fig. 22 B) NLRP3 protein expression and IL-1 β protein expression of pro-IL-1 β and mature-IL-1 β in cell lysates and cell culture supernatants of ASO-treated BMDM cells as analyzed by Western Blot

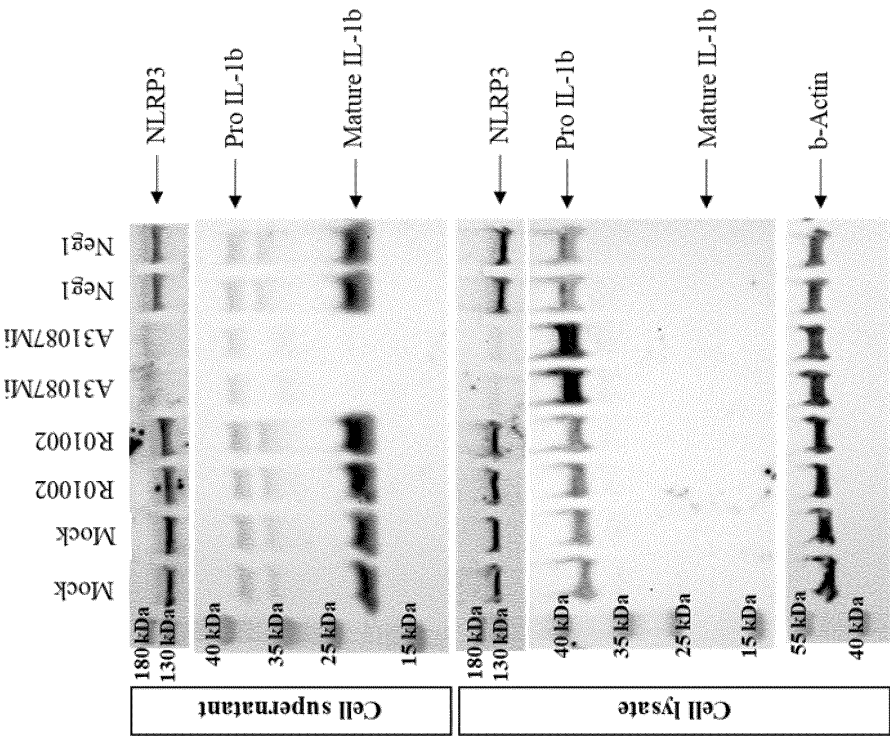


Fig. 23: Efficacy of selected mouse NLRP3-specific antisense oligonucleotides in mouse Raw246.7 cells

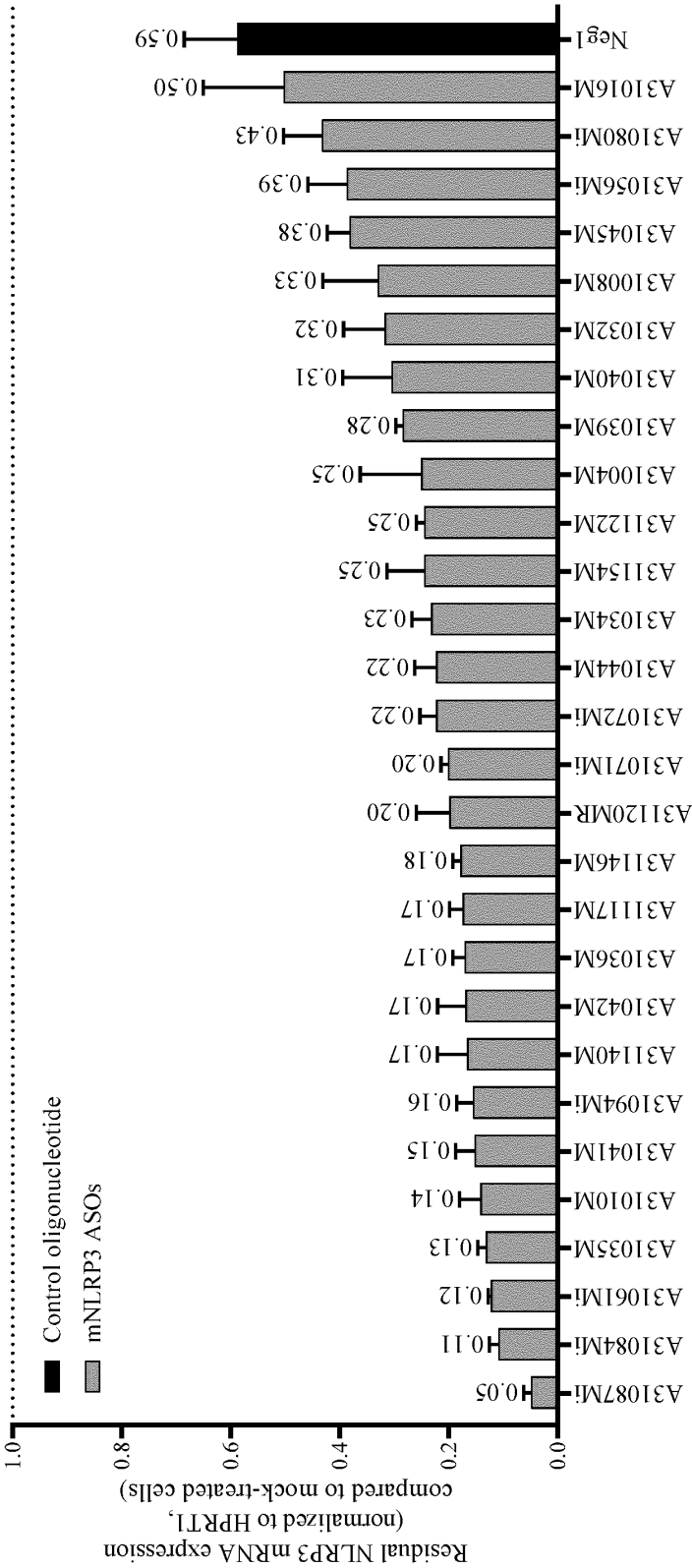


Fig. 24: Efficacy of selected mouse NLRP3-specific antisense oligonucleotides in mouse microglial IMG cells

