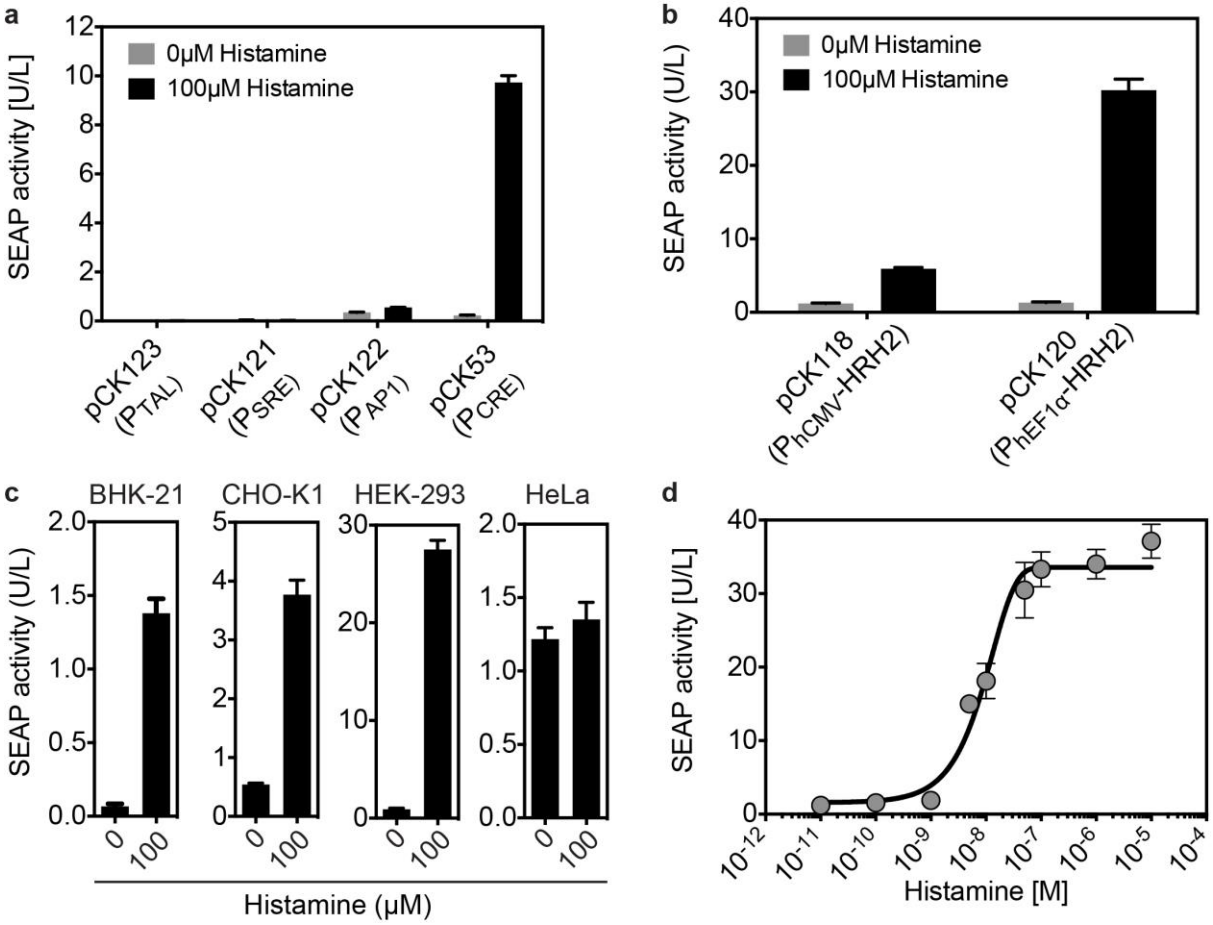
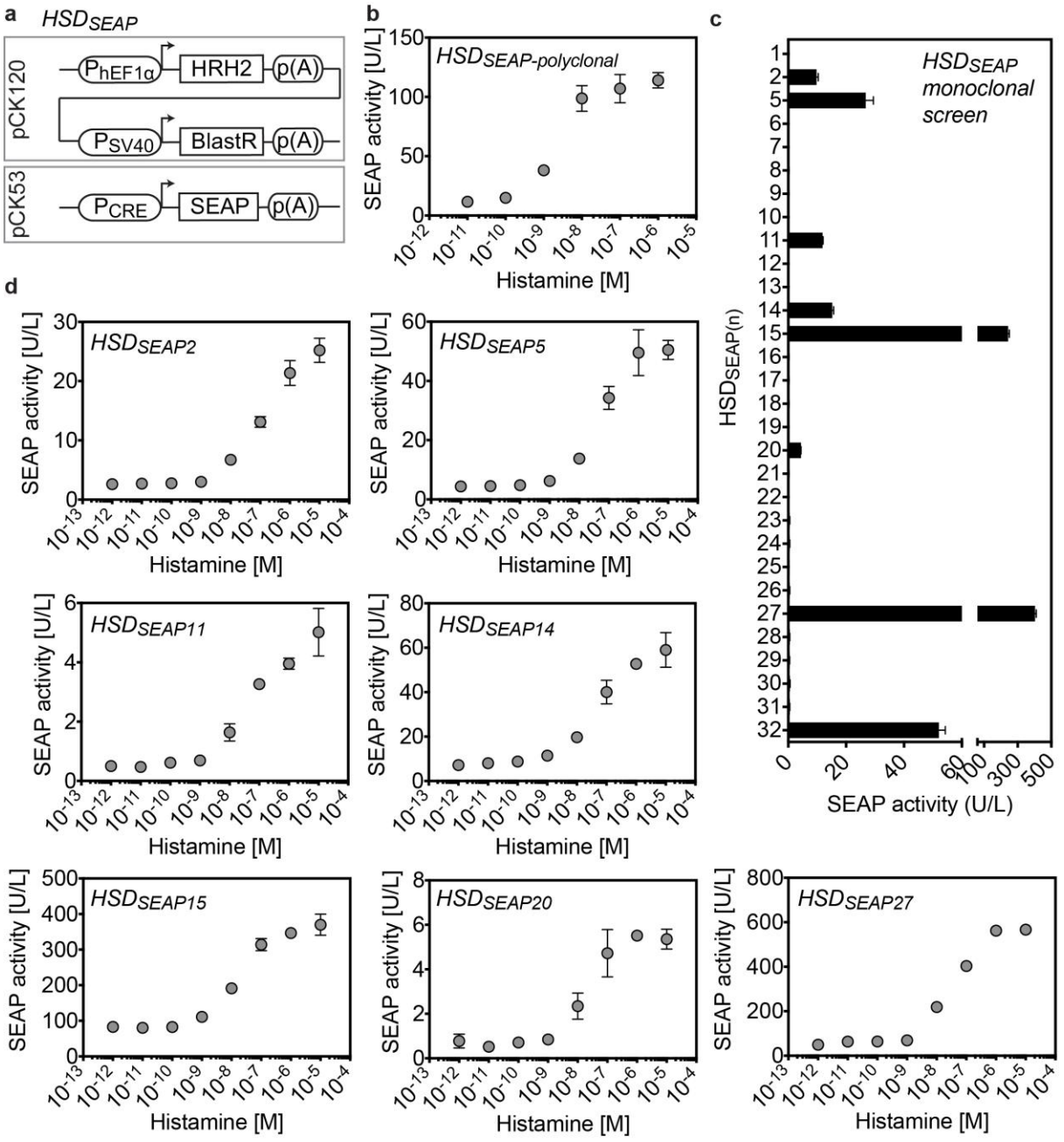
SUPPLEMENTARY FIGURES



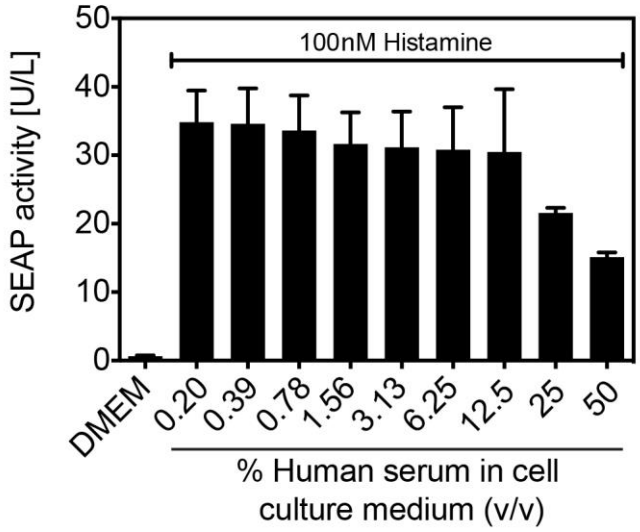
Supplementary Figure 1 | Optimization of histamine sensor device components.

a) Screening of activation of downstream signalling pathways in response to HRH2 induction. Cells were cotransfected with pCK118 and with plasmids encoding for different synthetic promoters pCK123 (P_{TAL}, minimal promoter), pCK121 (P_{SRE}, serum response element), pCK122 (P_{AP1}, activator protein 1) or pCK53 (P_{CRE}, cAMP-response element) before exposure to 100µM histamine for 24h. Thereafter, SEAP activity was assessed in the supernatant of cells. **b)** Influence of different constitutive promoters driving HRH2 expression in HEK293 cells. Cells were cotransfected with pCK118 or pCK120 and pCK53, before exposure to 100µM histamine for 24h. Thereafter, SEAP activity was assessed in the supernatant of cells. **c)** Performance of different mammalian cell lines. BHK21, CHO-K1, HEK293 and HeLa cells were cotransfected with pCK120 and pCK53 before induction with 100µM histamine for 24h. Thereafter, SEAP activity was quantified in culture supernatant. **d)** Histamine dose response of pCK120/pCK53-cotransfected HEK293 cells. pCK120/pCK53-cotransfected HEK293 cells were exposed the specific histamine concentrations before SEAP activity was assessed in the supernatant of cells.



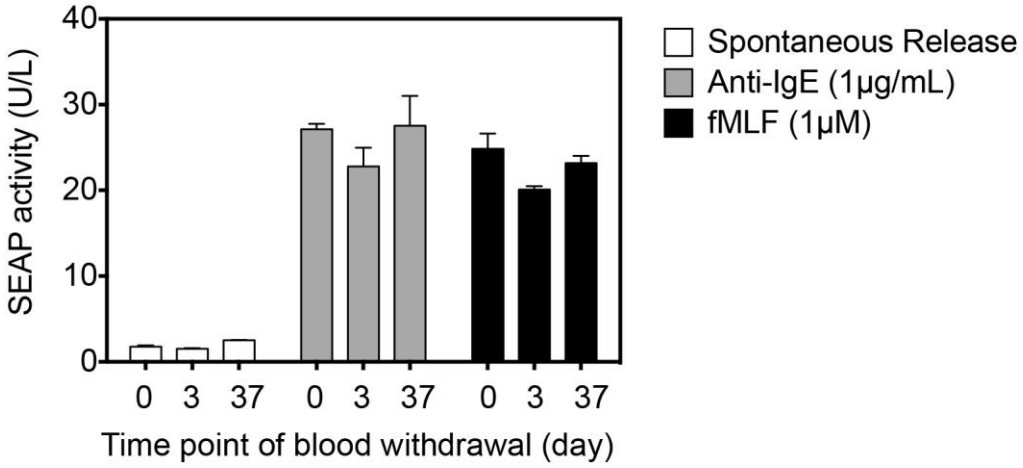
Supplementary Figure 2 | Production, screening and characterization of stable HSD_{SEAP} HEK293 cell lines.

a) Schematic illustration of stably introduced genetic components into HEK293 cells (see plasmid table S1 for details). **b)** Histamine dose response of the transgenic polyclonal cell line $HSD_{SEAP\text{-}polyclonal}$, which was selected for 3 weeks in DMEM supplemented with 20µg/mL blasticidin. **c)** Histamine-dependent SEAP expression of 32 monoclonal cell populations ($HSD_{SEAP(n)}$). Individual clones derived from $HSD_{SEAP\text{-}polyclonal}$ cells were exposed to 100nM histamine after SEAP activity was assessed in supernatant of cells. **d)** Histamine dose response curves of seven selected monoclonal $HSD_{SEAP(n)}$ cell populations. See Fig. 1d for HSD_{SEAP32} dose response.



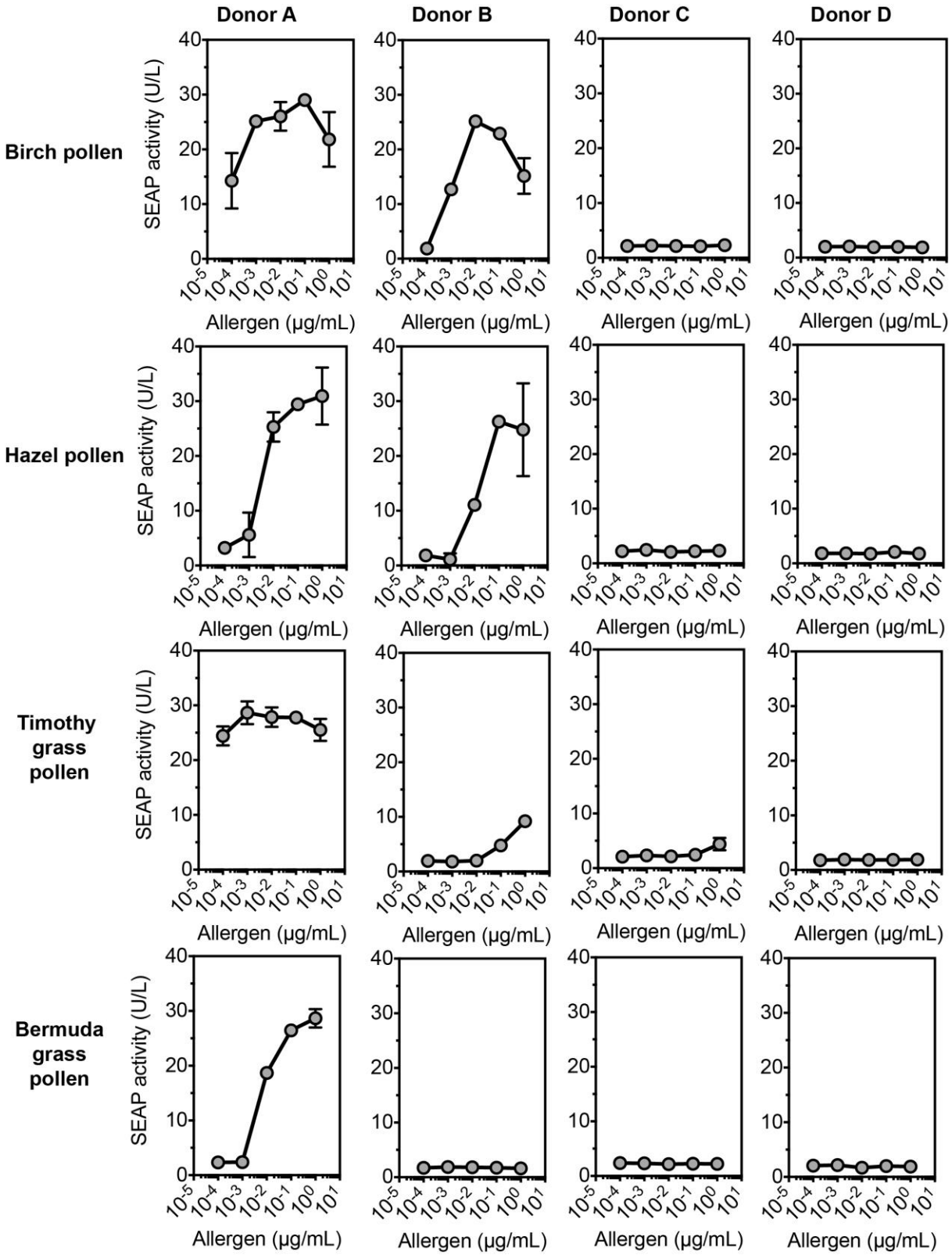
Supplementary Figure 3 | Influence of human serum on HSD_{SEAP32} cell response.

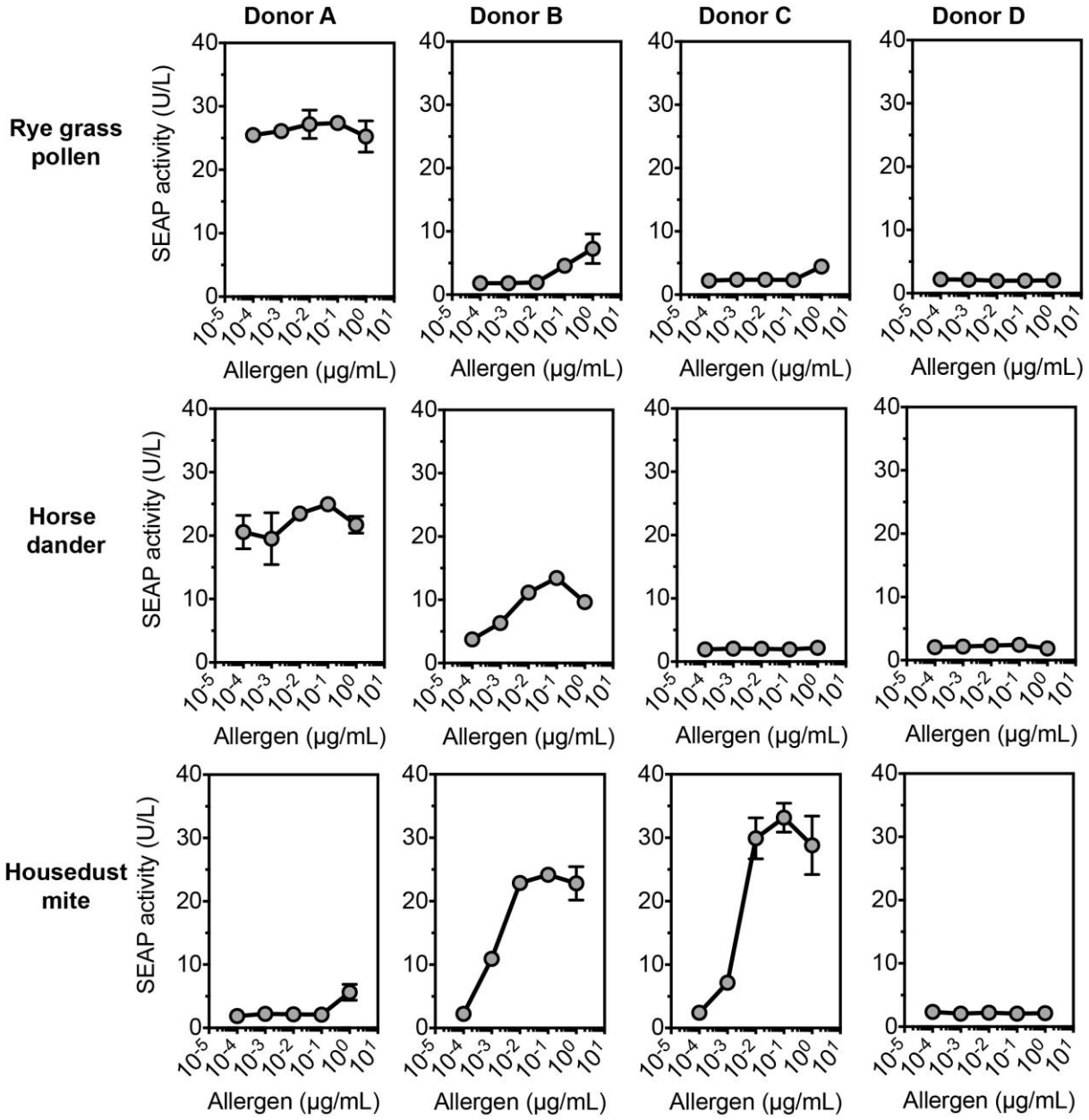
HSD_{SEAP32} cells were exposed to different dilutions of human serum in standard cell culture medium. Histamine was added to the mixture to a final concentration of 100nM. After 24h SEAP activity was assessed in the supernatant of cells.



Supplementary Figure 4 | Robustness of HSD_{SEAP32} cell responses.

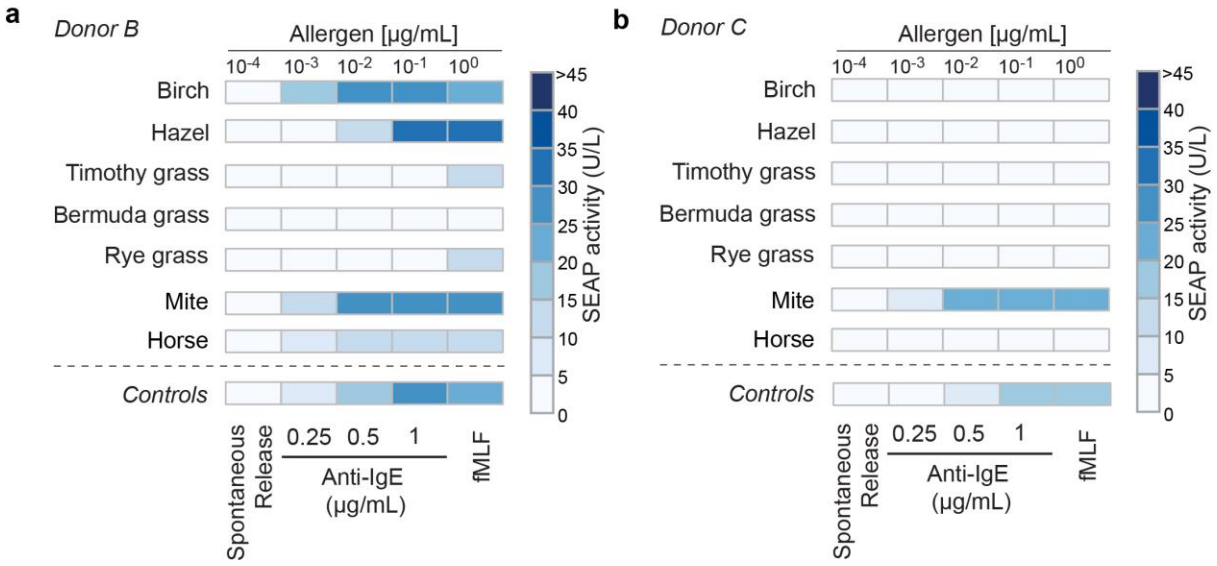
Whole blood samples taken from the same donor at three different time points,were exposed to either degranulation buffer alone, 1µg/mL anti-IgE or 1µM fMLF. Serum containing released histamine was directly added onto HSD_{SEAP32} cells, before SEAP was profiled in the culture supernatant. The mean of at least two histamine release assays per time point ± s.d. is shown.


Donor A
Donor B
Donor C
Donor D
Birch pollen
Hazel pollen
Timothy grass pollen
Bermuda grass pollen
SEAP activity (U/L)
Allergen (µg/mL)



Supplementary Figure 5 | Illustration of the intra-assay variation of allergy profiles shown in Figure 3.

Data of the allergy profiles obtained with HSD_{SEAP32} cells illustrated in Figure 3. The mean of at least two different histamine release assay per condition ± s.d. is shown.



Supplementary Figure 6 | Reproducibility of allergy profiles.

The same samples of the histamine release assay obtained for donors B and C shown in Figure 3 were retested after two freeze-thaw cycles using another batch of HSD_{SEAP32} cells. SEAP levels were quantified after 24h. Each cell of the heat map represents the mean of at least two histamine release assays.

SUPPLEMENTARY TABLE

Supplementary Table 1. Plasmids used and designed in this study

Plasmid	Description and Cloning Strategy	Reference or Source
pcDNA3.1(+)	Mammalian expression vector (P_{hCMV}-MCS-pA).	Life Technologies
pSEAP2-basic	SEAP-containing vector (MCS-SEAP-pA).	Clontech
pSEAP2-control	Constitutive SEAP expression vector (P_{SV40}-SEAP-pA).	Clontech
pSRE-luc	P_{SRE}-driven luciferase expression vector (P_{SRE}-luc-pA).	Clontech
pAP1-luc	P_{AP1}-driven luciferase expression vector (P_{AP1}-luc-pA).	Clontech
pTAL-luc	P_{TAL}-driven luciferase expression vector (P_{TAL}-luc-pA).	Clontech
pEV-UAS-H2B-Citrine	P_{UAS}-driven H2B-Citrine expression vector (P_{UAS}-H2B-Citrine-pA).	Sprinzak et al., 2010[1]
pSP16	P_{CREm}-driven SEAP expression vector (P_{CREm}-SEAP-pA).	Saxena et al., unpublished
pCK25	Constitutive mUTS expression vector ($P_{hEF1\alpha}$-mUTS-pA).	Kemmer et al., 2010[2]
pCK53	P_{CRE}-driven SEAP expression vector (P_{CRE}-SEAP-pA).	Kemmer et al., 2011[3]
pHRH2	pCMV-SPORT6-based vector containing HRH2 full-length cDNA (SB, cat. no. IRATp970G0878D).	GenBank: BC054510
pCK118	P_{hCMV}-driven HRH2 expression vector (P_{hCMV}-HRH2-pA). HRH2 was PCR-amplified from pHRH2 using oligonucleotides oCK140 (5'-GGAATTCCACCATGGCACCCAATGGCACAGC-3', *Eco*RI underlined) and oCK141 (5'-GCTCTAGATCATAATTCCTGG-CATGTGGTG-3', *Xba*I underlined) restricted with *Eco*RI/*Xba*I and cloned into corresponding sites (*Eco*RI/*Xba*I) of pcDNA3.1(+).	This work
pCK120	$P_{hEF1\alpha}$-driven HRH2 expression vector ($P_{hEF1\alpha}$-HRH2-pA). HRH2 was PCR-amplified from pHRH2 using oligonucleotides oCK140 and oCK141 restricted with *Eco*RI/*Xba*I and cloned into corresponding sites (*Eco*RI/*Xba*I) of pCK25.	This work
pCK121	P_{SRE}-driven SEAP expression vector (P_{SRE}-SEAP-pA). P_{SRE} was excised with *Not*I/*Hind*III from pSRE-luc and cloned into corresponding sites (*Not*I/*Hind*III) of pSEAP2-basic.	This work
pCK122	P_{AP1}-driven SEAP expression vector (P_{CRE}-SEAP-pA). P_{AP1} was excised with *Not*I/*Hind*III from pAP1-luc and cloned into corresponding sites (*Not*I/*Hind*III) of pSEAP2-basic.	This work
pCK123	P_{TAL}-driven SEAP expression vector (P_{CRE}-SEAP-pA). P_{TAL} was excised with *Not*I/*Hind*III from pTAL-luc and cloned into corresponding sites (*Not*I/*Hind*III) of pSEAP2-basic.	This work
pDA134	P_{CREm}-driven Citrine expression vector (P_{CREm}-Citrine-pA). Citrine was PCR-amplified from pEV-UAS-H2B-Citrine using oligonucleotides oDA183 (5'-CCGGAATTCCACCATGCCAGAGCCAGCGAAGTC-3', *Eco*RI underlined) and oDA184 (5'-GACCCGCGCGCTCAATGATGATGATGATGG-3', *BssH*II underlined), partially restricted with *Eco*RI/*BssH*II and cloned into corresponding sites (*Eco*RI/*BssH*II) of pSP16.	This work

Abbreviations: **Citrine**, improved version of the yellow fluorescent protein; **H2B**, histone H2B; **HRH2**, human histamine receptor H2; **Luc**, firefly luciferase; **MCS**, multiple cloning site; **mUTS**, mammalian urate-dependent transsilencer; **PCR**, polymerase chain reaction; **pA**, polyadenylation signal; **P_{UAS}**, synthetic mammalian promoter containing an upstream activation sequence; **P_{SRE}**, synthetic mammalian promoter containing a serum response element; **P_{AP1}**, synthetic mammalian promoter containing an activator protein 1-response element; **P_{TAL}**, TATA-like promoter region from herpes simplex virus lacking the enhancer

region; **P_{CRE}**, synthetic mammalian promoter containing a cAMP-response element; **P_{CREm}**, modified P_{CRE} variant; **P_{hCMV}**, human cytomegalovirus immediate early promoter; **$P_{hEF1\alpha}$**, human elongation factor 1 alpha promoter; **P_{SV40}**, simian virus 40 promoter; **SB**, Source Bioscience Lifesciences, Nottingham, UK; **SEAP**, human placental secreted alkaline phosphatase.

SUPPLEMENTARY REFERENCES

1. Sprinzak D, *et al.* Cis-interactions between Notch and Delta generate mutually exclusive signalling states. *Nature* **465**, 86-90 (2010).

2. Kemmer C, Gitzinger M, Daoud-El Baba M, Djonov V, Stelling J, Fussenegger M. Self-sufficient control of urate homeostasis in mice by a synthetic circuit. *Nat Biotechnol* **28**, 355-360 (2010).

3. Kemmer C, Fluri DA, Witschi U, Passeraub A, Gutzwiller A, Fussenegger M. A designer network coordinating bovine artificial insemination by ovulation-triggered release of implanted sperms. *Journal of controlled release* **150**, 23-29 (2011).