

## **Supplemental data**

### **S1: List of quantitatively analyzed publications**

1. Aaltonen TM, Jokinen EI, Lappivaara J, Markkula SE. 2000. Effects of primary-and secondary-treated bleached kraft mill effluents on the immune system and physiological parameters of roach. *Aquatic Toxicology*. 51:55–67.
2. Adel M, Amiri AA, Zorriehzahra J, Nematolahi A, Esteban MÁ. 2015. Effects of dietary peppermint (*Mentha piperita*) on growth performance, chemical body composition and hematological and immune parameters of fry Caspian white fish (*Rutilus frisii kutum*). *Fish Shellfish Immunol*. 45:841–847.
3. Ai Q, Mai K, Zhang L, Tan B, Zhang W, Xu W, Li H. 2007. Effects of dietary β-1, 3 glucan on innate immune response of large yellow croaker, *Pseudosciaena crocea*. *Fish Shellfish Immunol*. 22:394–402.
4. Akrami R, Gharaei A, Mansour MR, Galeshi A. 2015. Effects of dietary onion (*Allium cepa*) powder on growth, innate immune response and hemato-biochemical parameters of beluga (*Huso huso Linnaeus, 1754*) juvenile. *Fish Shellfish Immunol*. 45:828–834.
5. Albergoni V, Viola A. 1995. Effects of cadmium on catfish, *Ictalurus melas*, humoralimmune response. *Fish Shellfish Immunol*. 5:89–95.
6. Ali AO, Hohn C, Allen PJ, Ford L, Dail MB, Pruett S, Petrie-Hanson L. 2014. The effects of oil exposure on peripheral blood leukocytes and splenic melano-macrophage centers of Gulf of Mexico fishes. *Mar Pollut Bull*. 79:87–93.
7. Arkoosh MR, Boylen D, Dietrich J, Anulacion BF, Gina Ylitalo, Bravo CF, Johnson LL, Loge FJ, Collier TK. 2010. Disease susceptibility of salmon exposed to polybrominated diphenyl ethers (PBDEs). *Aquatic Toxicology*. 98:51–59.
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9. Arkoosh MR, Van Gaest AL, Strickland SA, Hutchinson GP, Krupkin AB, Dietrich JP. 2015. Dietary Exposure to Individual Polybrominated Diphenyl Ether Congeners BDE-47 and BDE-99 Alters Innate Immunity and Disease Susceptibility in Juvenile Chinook Salmon. *Environ Sci Technol*. 49:6974–6981.
10. Bado-Nilles A, Quentel C, Auffret M, Le Floch S, Gagnaire B, Renault T, Thomas-Guyon H. 2009. Immune effects of HFO on European sea bass, *Dicentrarchus labrax*, and Pacific oyster, *Crassostrea gigas*. *Ecotoxicol Environ Saf*. 72:1446–1454.
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- functions in the European sea bass, *Dicentrarchus labrax* (Linné). *Ecotoxicol Environ Saf.* 74:1896–1904.
12. Bado-Nilles A, Techer R, Porcher JM, Geffard A, Gagnaire B, Betouille S, Sanchez W. 2014. Detection of immunotoxic effects of estrogenic and androgenic endocrine disrupting compounds using splenic immune cells of the female three-spined stickleback, *Gasterosteus aculeatus* (L.). *Environ Toxicol Pharmacol.* 38:672–683.
  13. Baier-Anderson C, Anderson R. 2000. Suppression of superoxide production by chlorothalonil in striped bass (*Morone saxatilis*) macrophages: the role of cellular sulphydryls and oxidative stress. *Aquat Toxicol.* 50:85–96.
  14. Bakirel T, Keleş O, Karataş S, Özcan M, Türkmen G, Candan A. 2005. Effect of linear alkylbenzene sulphonate (LAS) on non-specific defence mechanisms in rainbow trout (*Oncorhynchus mykiss*). *Aquatic Toxicology.* 71:175–181.
  15. Banerjee S, Mitra T, Purohit GK, Mohanty S, Mohanty BP. 2015. Immunomodulatory effect of arsenic on cytokine and HSP gene expression in *Labeo rohita* fingerlings. *Fish Shellfish Immunol.* 44:43–49.
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  18. Benchalgo N, Gagne F, Fournier M. 2014. Immunotoxic effects of an industrial waste incineration site on groundwater in rainbow trout (*Oncorhynchus mykiss*). *J Environ Sci (China).* 26:981–990.
  19. Betouille S, Duchiron C, Deschaux P. 2000. Lindane increases in vitro respiratory burst activity and intracellular calcium levels in rainbow trout (*Oncorhynchus mykiss*) head kidney phagocytes. *Aquatic Toxicology.* 48:211–221.
  20. Betouille S, Etienne JC, Vernet G. 2002. Acute Immunotoxicity of Gallium to Carp (*Cyprinus carpio* L.). *Bulletin of Environmental Contamination and Toxicology.* 68:817–823.
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26. Cabas I, Liarte S, García-Alcázar A, Meseguer J, Mulero V, García-Ayala A. 2012. 17beta-Ethynodiol alters the immune response of the teleost gilthead seabream (*Sparus aurata* L.) both in vivo and in vitro. *Developmental & Comparative Immunology*. 36:547–556.
27. Carlson EA, Li Y, Zelikoff JT. 2002. The Japanese medaka (*Oryzias latipes*) model: applicability for investigating the immunosuppressive effects of the aquatic pollutant benzo[a]pyrene (BaP). *Mar Environ Res*. 54:565–568.
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31. Castro R, Zou J, Secombes CJ, Martin SAM. 2011. Cortisol modulates the induction of inflammatory gene expression in a rainbow trout macrophage cell line. *Fish Shellfish Immunol*. 30:215–223.
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35. Chen X, Yao G, Hou Y. 2005. Pentachlorophenol reduces B lymphocyte function through proinflammatory cytokines in *Carassius auratus*. *Food and Chemical Toxicology*. 43:239–245.
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40. Connelly H, Means JC. 2010. Immunomodulatory Effects of Dietary Exposure to Selected Polycyclic Aromatic Hydrocarbons in the Bluegill (*Lepomis macrochirus*). *International Journal of Toxicology*. 29:532–545.
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42. Cortés R, Teles M, Trídico R, Acerete L, Tort L. 2013. Effects of Cortisol Administered through Slow-Release Implants on Innate Immune Responses in Rainbow Trout (*Oncorhynchus mykiss*). *International Journal of Genomics*. 2013:1–7.
43. Cuesta A, Esteban MA, Meseguer J. 2002. Levamisole is a potent enhancer of gilthead seabream natural cytotoxic activity. *Vet Immunol Immunopathol*. 89:169–174.
44. Cuesta A, Laiz-Carrión R, Martín del Río MP, Meseguer J, Miguel Mancera J, Ángeles Esteban M. 2005. Salinity influences the humoral immune parameters of gilthead seabream (*Sparus aurata* L.). *Fish Shellfish Immunol*. 18:255–261.
45. Cuesta A, Meseguer J, Esteban MÁ. 2008. Effects of the organochlorines p,p'-DDE and lindane on gilthead seabream leucocyte immune parameters and gene expression. *Fish Shellfish Immunol*. 25:682–688.
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## **Supplemental data**

### **S2: frequency in the use of immune parameters / methods** (article-based analysis)

immune parameters / methods	frequency used
phagocytic activity	195
expression of immune-related genes	149
respiratory burst activity	118
lysozyme activity	77
leukocyte number	76
challenge mortality	61
antibodies / Ig's	49
total lymphocytes	47
nitric oxide concentration	33
haemolytic complement activity	31
Immunologic organ index	22
peroxidase activity	22
ELISA, mainly IgM	21
total thrombocytes	17
C3 content	14
lymphocyte proliferation	12
PFC assay	11
IgM secretion	10
WBC count	10
ACP activity	9
bactericidal activity	9
Ceruloplasmin activity	9
apoptosis (blood lymphocytes)	8
leukocyte apoptosis	8
leukocyte proliferation	8
superoxide dismutase activity	8
lymphoblastic proliferation	7
chemiluminescence response	6
mitogenic response (HK leukocytes)	6
leukocyte proliferation	5
antibacterial activity (serum & mucus)	4
FACS	4
heamatokrit	4
lymphocyte transformation	4
proliferation index (HK cells)	4

Antiprotease activity	3
bacterial agglutination	3
blastogenic response	3
CRP level	3
haemagglutination test	3
heaptosomatischer index	3
MHC	3
spleen cell number	3
thymocyte viability	3
bacterial load	2
caspase activity	2
HK cell number	2
myeloperoxidase content	2
total lymphoid cells	2
blastogenesis of surface IgM presenting leukocytes	1
cell adhesion property of intestinal macrophages	1
chemotaxis activity (HK leukocytes)	1
Degranulation	1
Extracellular trap release	1
gene chip	1
intercellular peroxidase content	1
intracellular killing capacity of intestinal macrophages	1
Leucocrit	1
lipid analyses	1
lipid peroxidation in plasma	1
lymphokine production (HK lymphocytes)	1
MPO activity	1
myeloperoxidase release of intestinal macrophages	1
Natural cytotoxic activity	1
NCC cytotoxic activity	1
necrosis (thymocytes)	1
NET	1
NHC activity	1
oxygenase activity	1
pERK1/2 expression (splenocytes)	1
phagocyte migration (sup+)	1
phagocyte migration (ZAS)	1
plasma protein	1
relative spleen weight	1
RNI production	1
RNS production	1
serum albumin	1

Serum peroxidase content	1
serum protein	1
serum TNF-alpha content	1
splenocyte proliferation	1
splenocyte senescence	1
splenocytes concentration	1
splenocytes viability	1
T cell proliferation	1
TNF-alpha release of intestinal macrophages	1
total erythrocytes	1
total lysozyme (plasma)	1
total plasma protein	1
total sIg (blood)	1
trophont number	1
viral titer	1
xenoma counts	1
xenoma size	1
In total	1160

## **Supplemental data**

### **S3: Chemical grouping**

This table shows how we categorized the different groups of chemicals that were used in the quantitatively analyzed 241 publications. We would like to emphasize that this grouping is based on an ecotoxicological approach, in which chemicals are mostly categorized according to their use or their most prominent effects. We are aware that some of the chemicals may have more than one mode of action, e.g. the pesticide tributyltin could also be classified as EDC, or some of the pharmaceuticals could also be put in other categories. There are different ways to solve this, which have all their own limitations. Thus, we decided to go for the ecotoxicological approach.

#### **hormones/EDCs**

11-ketoandrostenedione

11-ketotestosterone

17alpha,20beta-dihydroxy progesterone

3-methylcholanthrene

aldosterone

beta-endorphin

bisphenol A

corticosterone

cortisol

cortisone

dexamethasone

estradiol

estrone

ethinylestradiol

hydrocortisone

levonorgestrel

medroxyprogesterone acetate

morphine

methyltestosterone

nonylphenol

PBDE mix

permethrin

progesterone

trenbolone

testosterone

trenbolone acetat

triiodothyronine

**pesticides**

acetochlor  
atrazine  
bifenthrin  
bis(*tri-n*-butyltin)oxide  
butachlor  
carbendazim  
chlorothalonil  
chlormpyrifos  
*cis*-bifenthrin  
cycloheximide  
cypermethrin  
deltamethrin  
diazinon  
dibutyltin  
endosulfan  
esfenvalerate  
glyphosate  
herbicide mix (atrazine, simazine, diuron, isoproturon)  
lindane  
malathion  
metriphonate  
*o,p'*-DDE  
*p,p'*-DDE  
paraquat  
pentachlorophenol  
permethrin  
piperonyl  
pyraclofos  
pyrethroid  
tributyltin

**nutrients/vitamins**

*aloe barbadensis*  
beta-glucan  
chitin  
chitosan  
*eclipta alba* leaf extract  
fructooligosaccharide  
inulin  
lactoferrin  
lipopolysaccharide  
microcystin-LR

*mucor cirinelloides*

n-3 hufa treated yeast  
onion  
peppermint  
probiotic bacteria  
propolis  
raffinose  
retinol acetate  
salinity  
*scutellaria radix*  
vitamin C  
vitamin D3 (cholecalciferol)  
vitamin E  
whole cell yeast (*saccharomyces cerevisiae*)

**metals**

arsenic  
cadmium  
chromium  
copper  
copper sulfate  
gallium  
lead acetate  
lead nitrate  
mercury chloride  
methyl mercury  
nickel  
quantum dots (CdS/CD)  
sodium arsenite  
titan (nanosized particles)  
titanium dioxide (nanosized particles)  
trioxide arsenic

**PCBs/PAHs/organics**

2-phenoxyethanol  
aroclor 1245  
aroclor 1248  
aroclor 1254  
BDE-47  
BDE-99  
benz(a)pyrene-7,8-dihydrodiol  
benzo(a)pyrene  
BPDE

clophen A50  
dimethylbenz(a)anthracene  
diverse PAHs  
methylchloranthrene  
PAH mixture  
PCB 126  
phenanthrene  
putrescin  
retene  
2,3,7,8-tetrachlorodibenzo-p-dioxin  
tert-butyl-hydroperoxide

### **pharmaceuticals**

anatoxin-a  
benzocaine  
creosote  
cyclophosamide  
dibutyl phthalate  
diclofenac  
levamisole  
tricaine methanesulfonate  
oxytetracycline  
phenanthrene  
potassium permanganate  
quinaldine sulphate

### **field**

effluent  
effluent, reus water  
field  
groundwater  
municipal effluent  
naphtetic acids (from oil-sand water)  
oil sands  
oil-sand influenced water  
polluted estuarine sediment  
sediment extract  
sediments  
tertiary-treated municipal sewage effluent  
waste water effluents  
wastewater effluent (primary treated )

**others**

1-methyl-3-octylimidazolium bromide  
3-methylcholanthrene  
actinomycin D  
aflatoxin b1  
alkylbenzensulfaphonat  
arabian crude oil  
beta-mercapto-ethanol treated yeast  
cadmium chloride  
carbon nanotubes  
chlorine  
diethylhexyl phthalate  
dimethyl sulfoxide  
formalin  
heavy oil  
hypoxia  
iranian heavy crude oil  
light oil  
mercuric chloride  
naphthenic acids  
oil  
perfluorooctanoic acid  
perfluorooctanesulfonic acid  
sodium telluride  
spermidine  
spermine  
sulforic acid  
zinc chloride

## **Supplemental data**

### **S4: List of analyzed immune-related genes by means of qRT-PCR (article-based analysis)**

genes	frequency used
IL (Interleukin)	91
TNF (Tumor necrosis factor)	40
IFN (Interferone)	26
CXC (chemokine receptor)	20
MX (myxovirus resistance)	15
C3 (complement component 3)	13
TGF (Transforming growth factor)	11
CC-chemokine	10
IgM (Immunoglobulin M)	8
iNOS (Nitric oxide synthase)	8
MHC (major histocompatibility complex)	7
IGF (Insulin-like growth factor)	6
Lysozyme	6
COX (Cyclooxygenase)	5
Bcl2 (B-cell lymphoma 2)	4
CAT (chloramphenicol acetyltransferase)	4
CCL	4
SOCS (suppressor of cytokine signaling)	4
C4 (complement component 4)	3
NF-kB-inh (Nuclear factor NF-kappa-B inhibitor)	3
NF-kb2 (Nuclear factor NF-kappa-B p100 subunit)	3
SOD (Superoxide dismutase)	3
TCR (T-cell receptor)	3
TLR (Toll-like receptor)	3
C9 (complement component 9)	2
Caspase	2
Factor B	2
Factor H	2
GPx (Glutathione peroxidase 2)	2
GR (glucocorticoid receptor)	2
GST (Glutathione S-transferase)	2
Hep (hepcidine)	2
ISG (interferon-stimulated gene)	2
Macroph.stimul.1	2
NCCRP-1 (non-specific cytotoxic cell receptor protein 1)	2
Nkapl (NFKB activating protein -like)	2
Rag (recombination-activating gene)	2
SAA (Serum amyloid A)	2
Ucp2 (Mitochondrial uncoupling protein 2)	2
Arg2 (Arginase, type II)	1
A-SAA (serum amyloid A)	1

BD (beta-defensin)	1
beta-hemoglobin	1
C1r/s (complement component 1)	1
C7 (complement component 7)	1
C8 (complement component 8)	1
CCR7 (C-C chemokine receptor type 7)	1
CD28 (cluster of differentiation 28)	1
CD3 (cluster of differentiation 3)	1
CD4 (cluster of differentiation 4)	1
CD8 (cluster of differentiation 8)	1
CFP (complement factor properdin)	1
CSF-1R (Colony stimulating factor 1 receptor)	1
CTSL (Cathepsin L)	1
Cyclin	1
Elastase2	1
F2 (coagulation factor 2)	1
Ferritin M	1
G-CSF (Granulocyte-colony stimulating factor)	1
g-type lysozyme	1
hamp1 (hepcidin antimicrobial peptide 1)	1
HMGB1 (High-mobility group protein B1)	1
HP	1
IFR3 (interferon regulatory factor 3)	1
Keap1 (Kelch-like ECH-associated protein 1)	1
MBL-2 (Mannan-binding lectin 2)	1
mt (metallothionein)	1
NADPHoxid. (nicotinamide adenine dinucleotide phosphate-oxidase)	1
NOX	1
NRAMP (natural resistance-associated macrophage protein)	1
NrF2 (Nuclear factor (erythroid-derived 2)-like 2)	1
Pannexin1	1
PBX (pre-B-cell leukaemia transcription factor)	1
ptgs1 (prostaglandin G/H synthase 1)	1
Rela (NFKB subunit)	1
SQSTM1 (sequestosome-1)	1
TCPBP (trout C-polysaccharide binding protein)	1
TF (transfer factor)	1
TRAF3 (TNF receptor-associated factor 3)	1
Vig-8 (vaccinia immune globulin-8)	1
yIP (gamma-interferon-inducible gene)	1

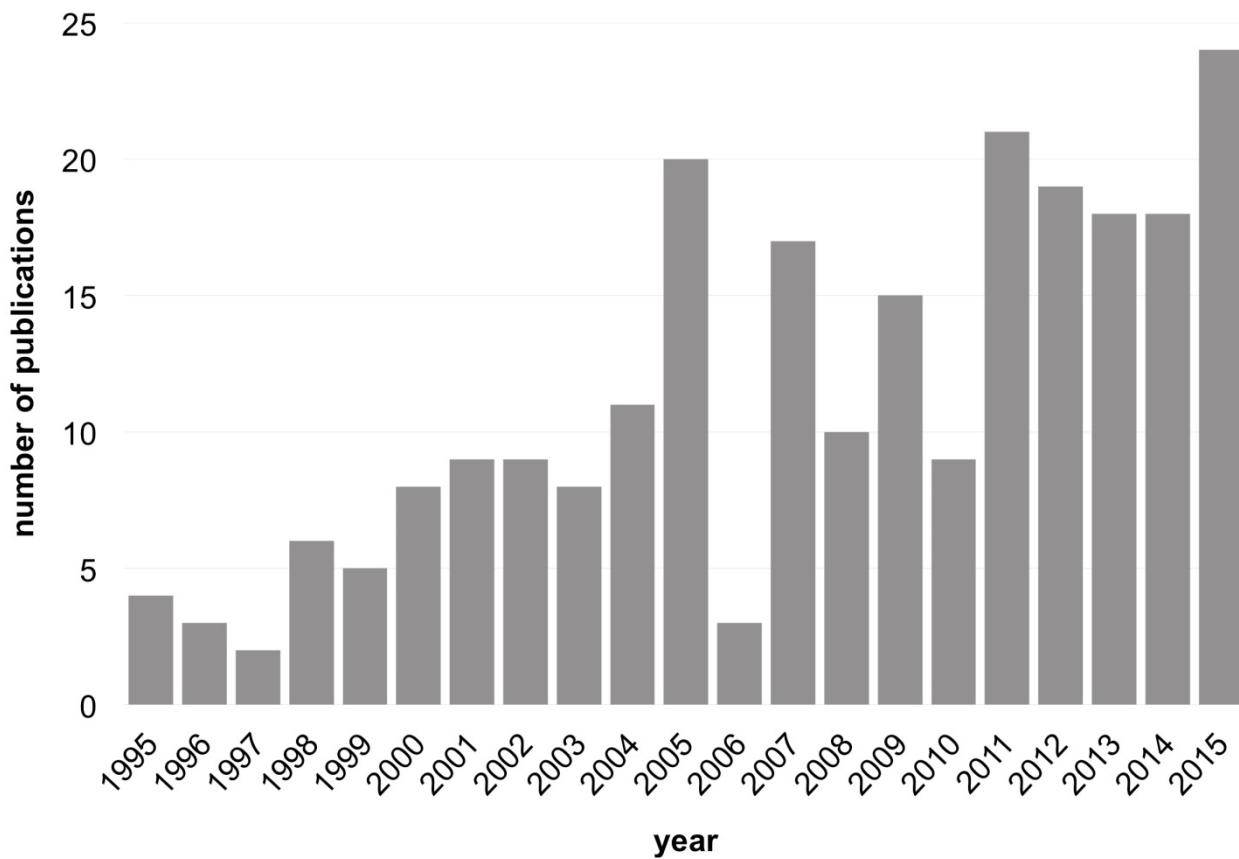


Fig 1

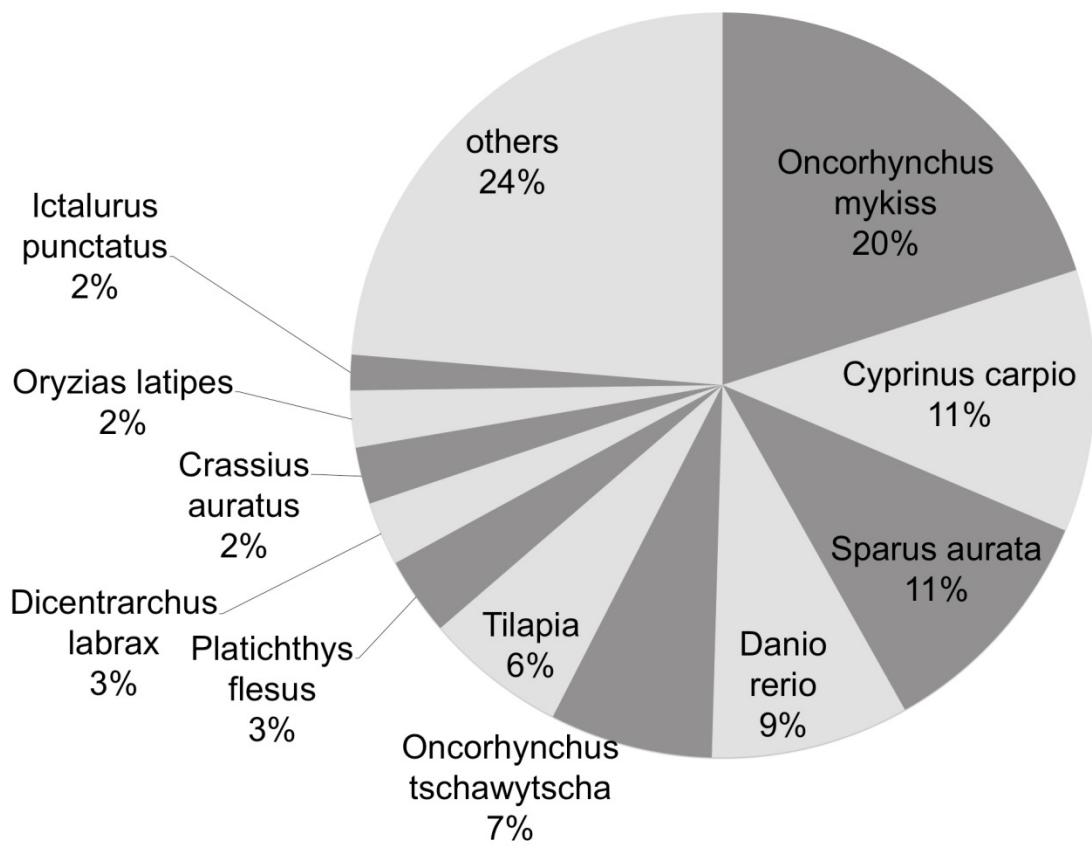


Fig. 2

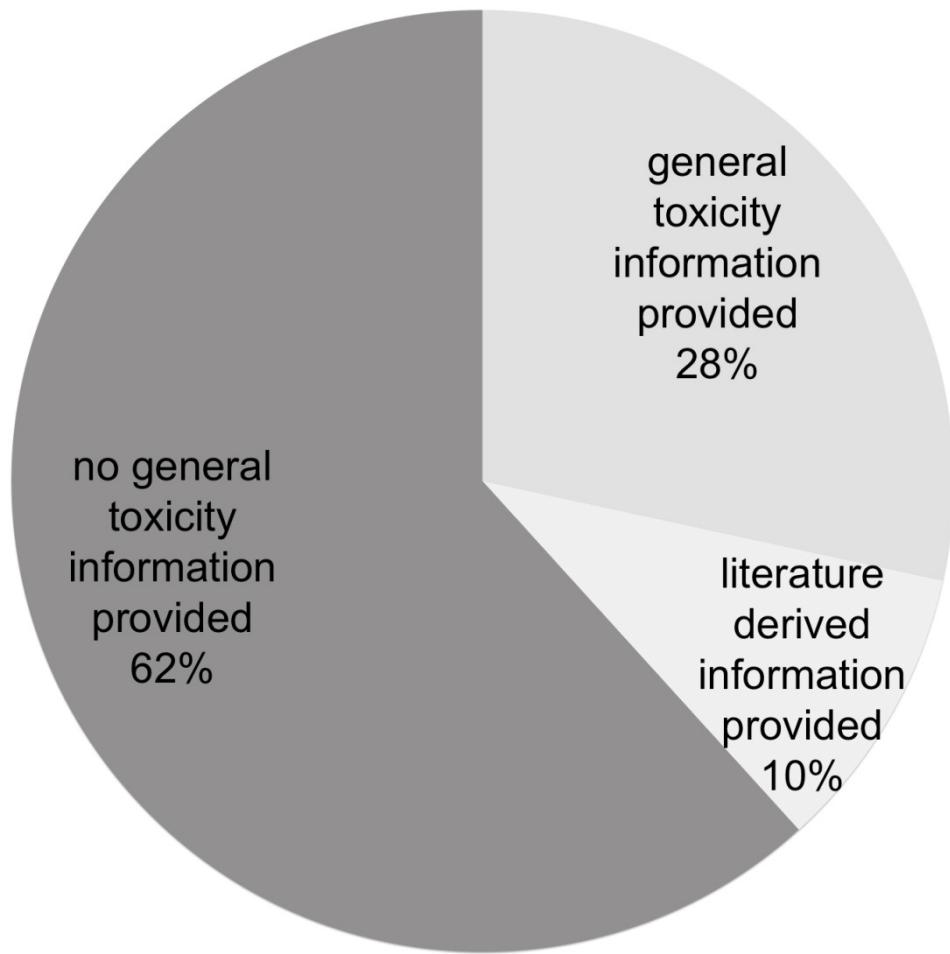


Fig 3

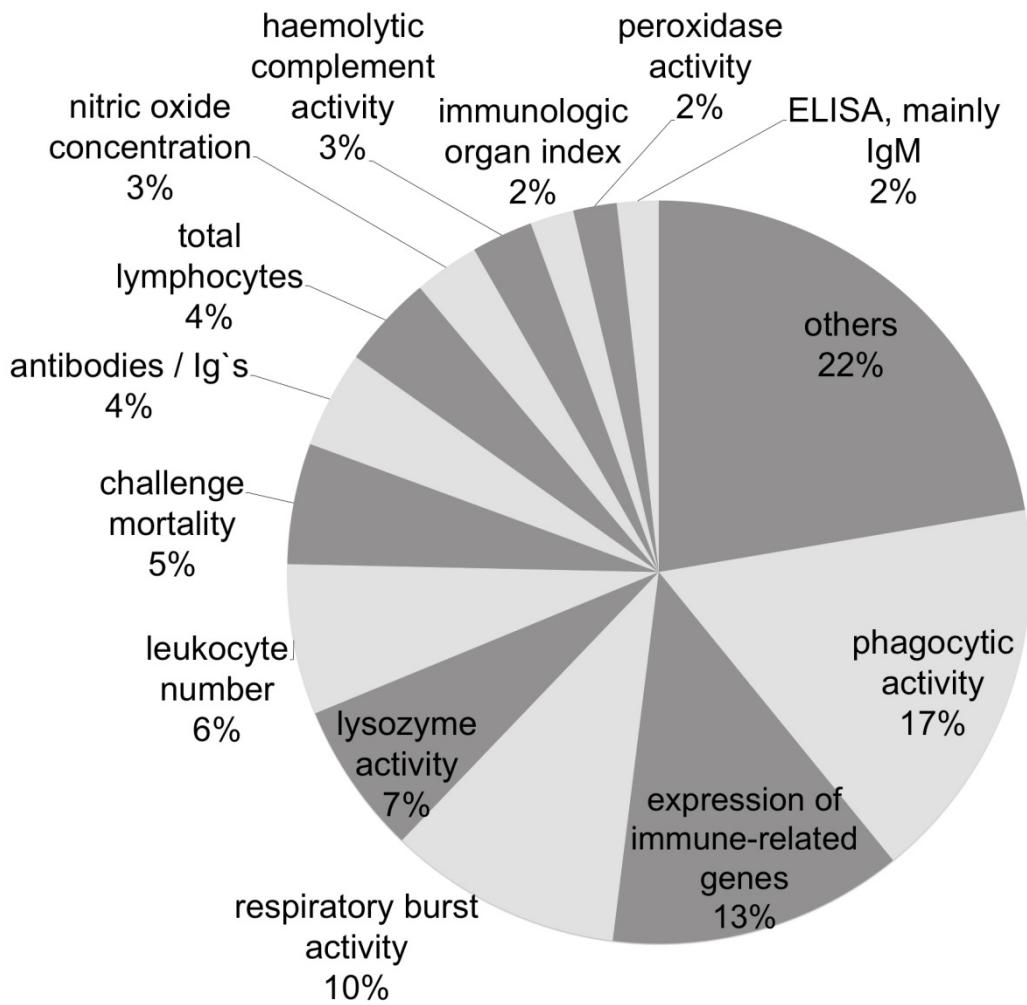


Fig 4

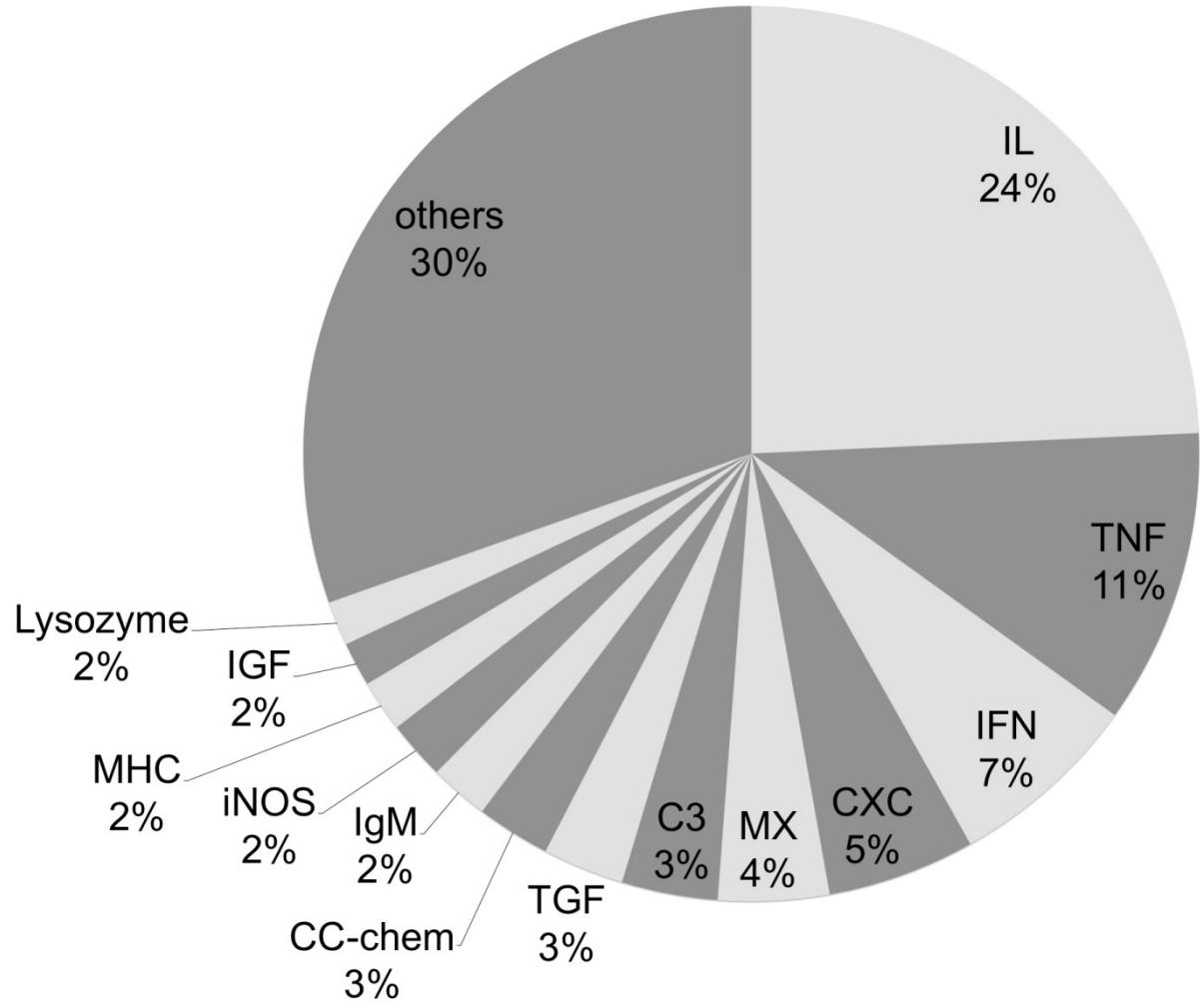


Fig 5

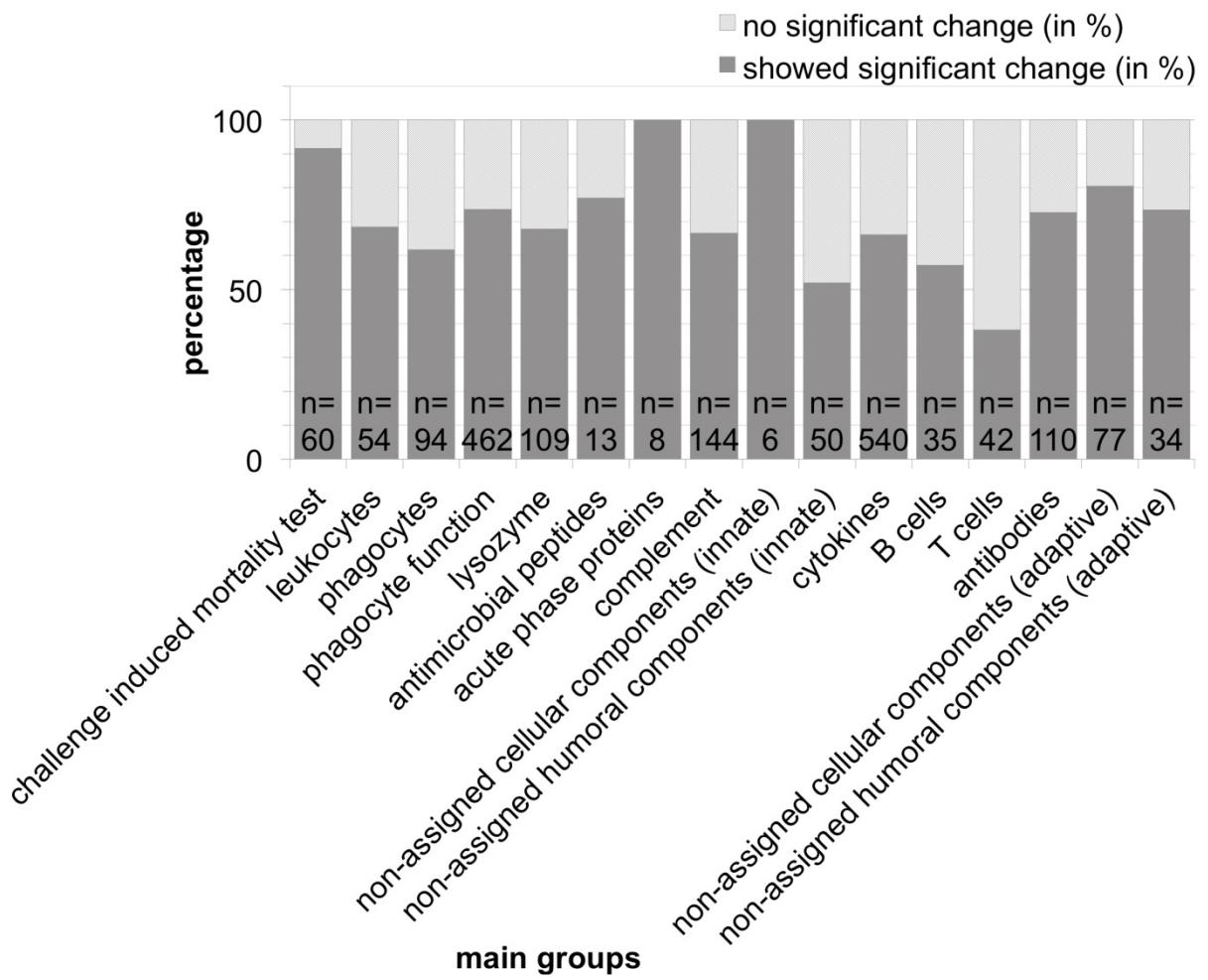


Fig 6

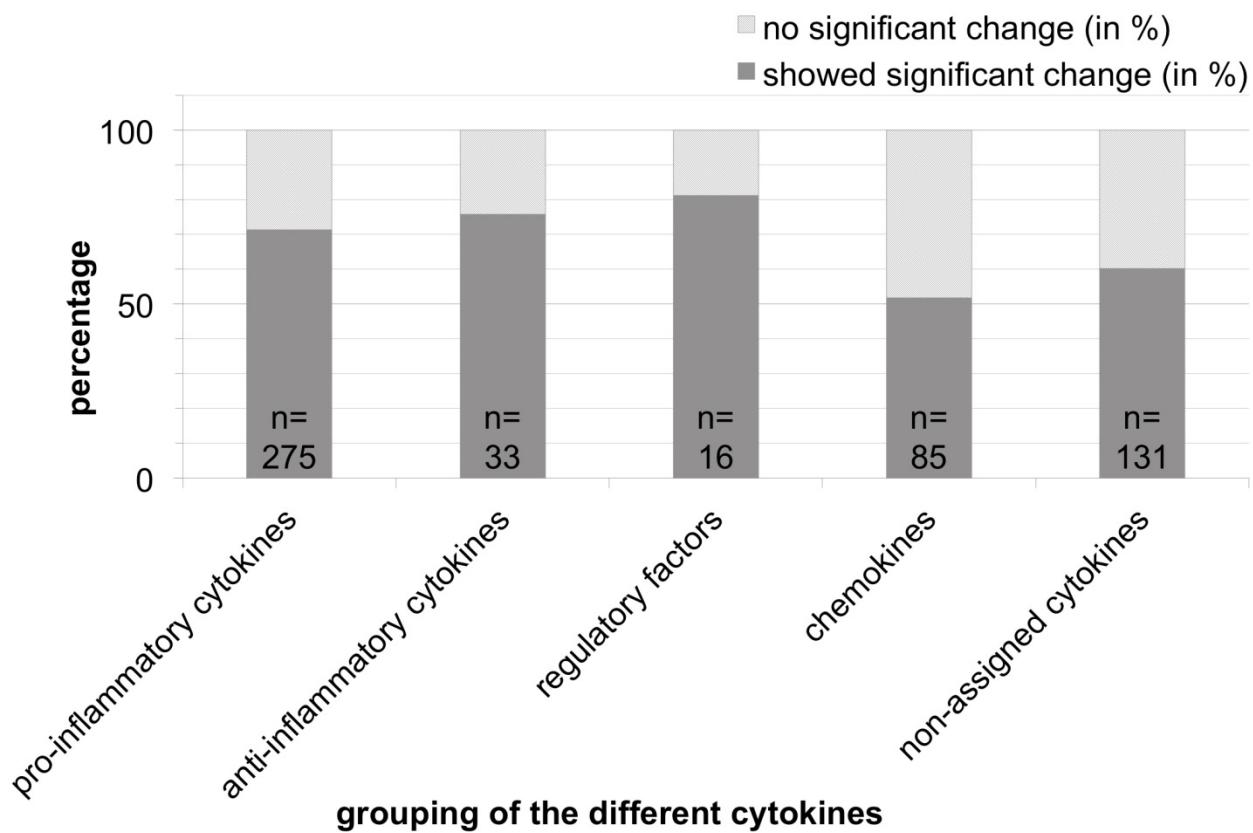


Fig 7

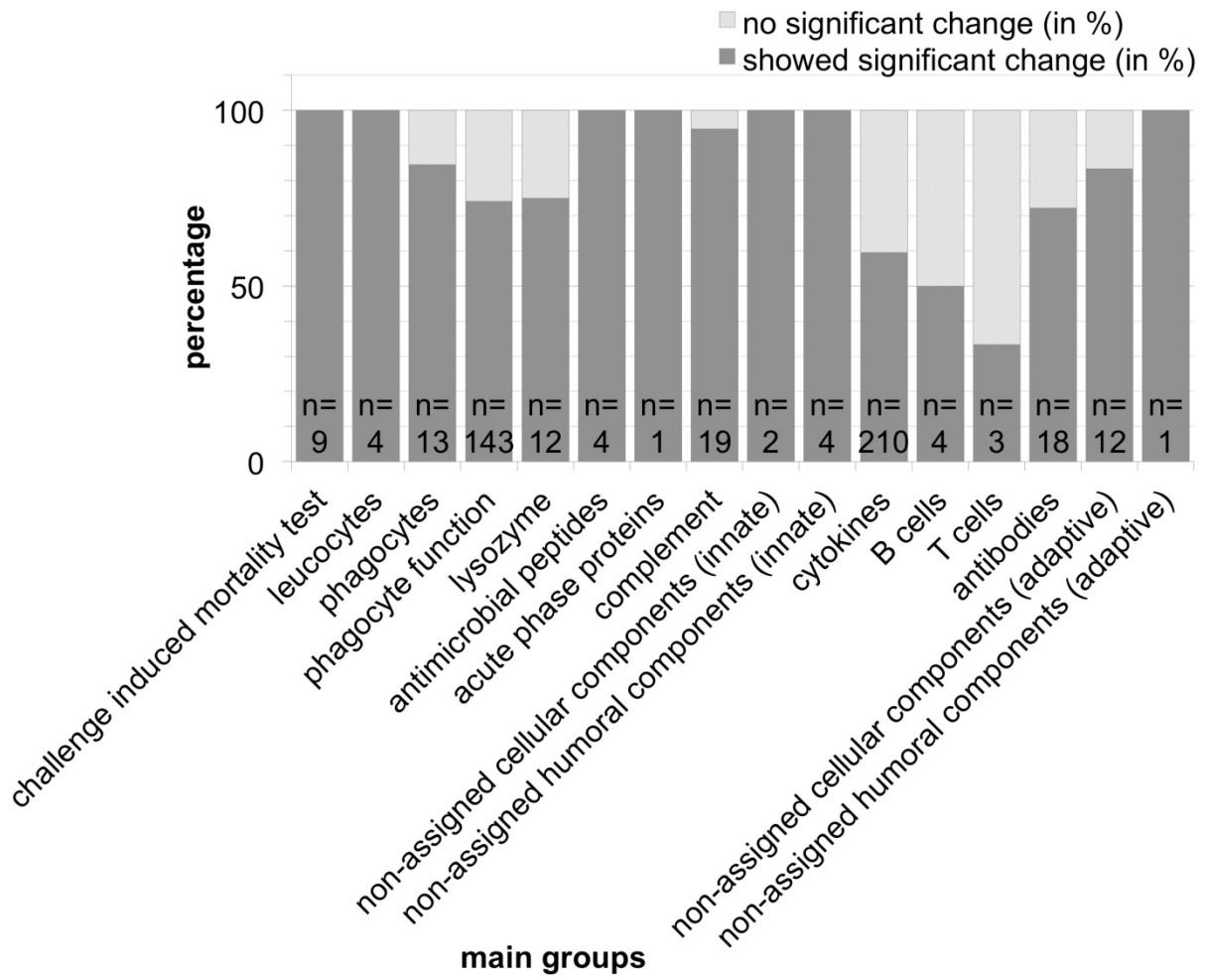


Fig 8

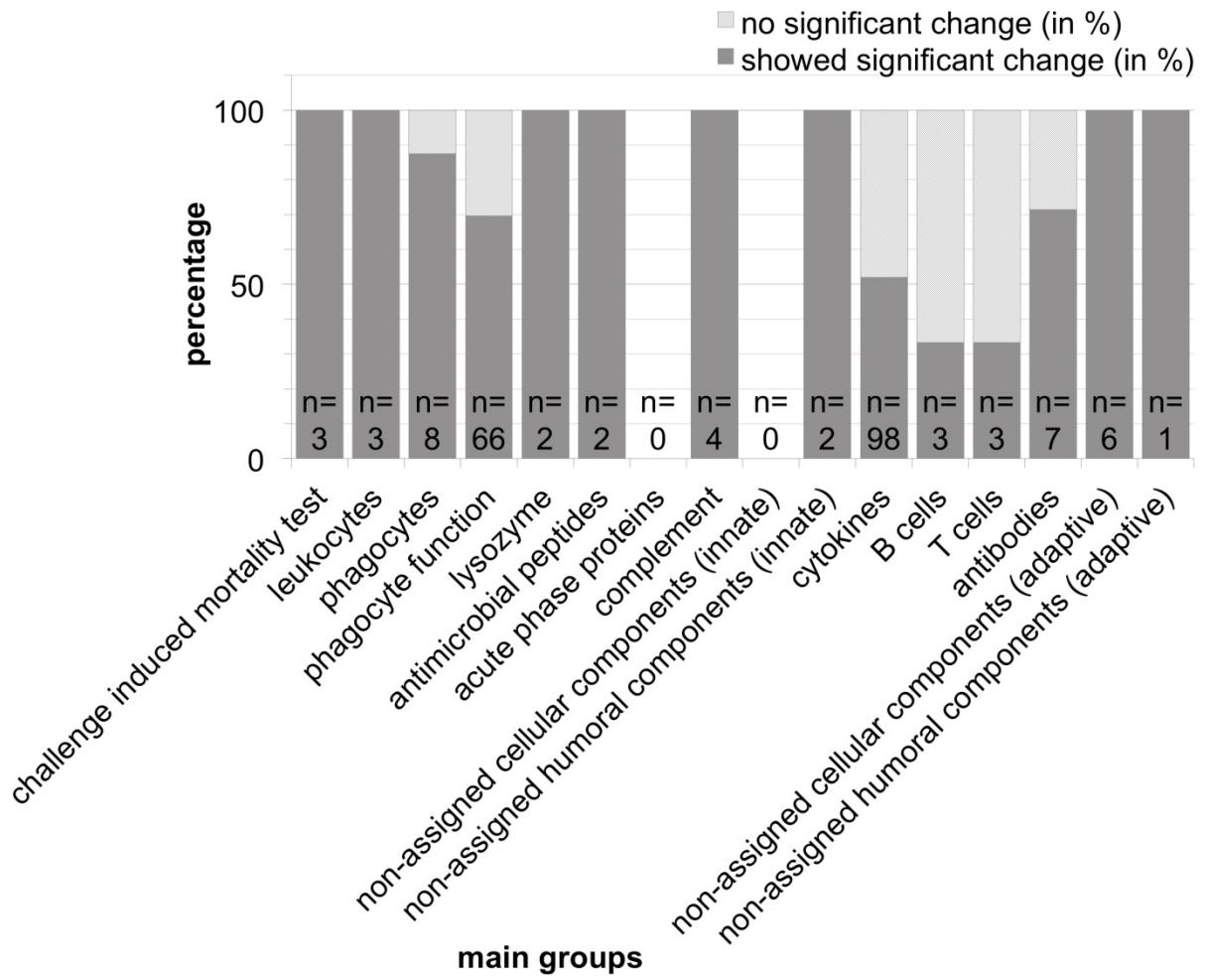


Fig 9

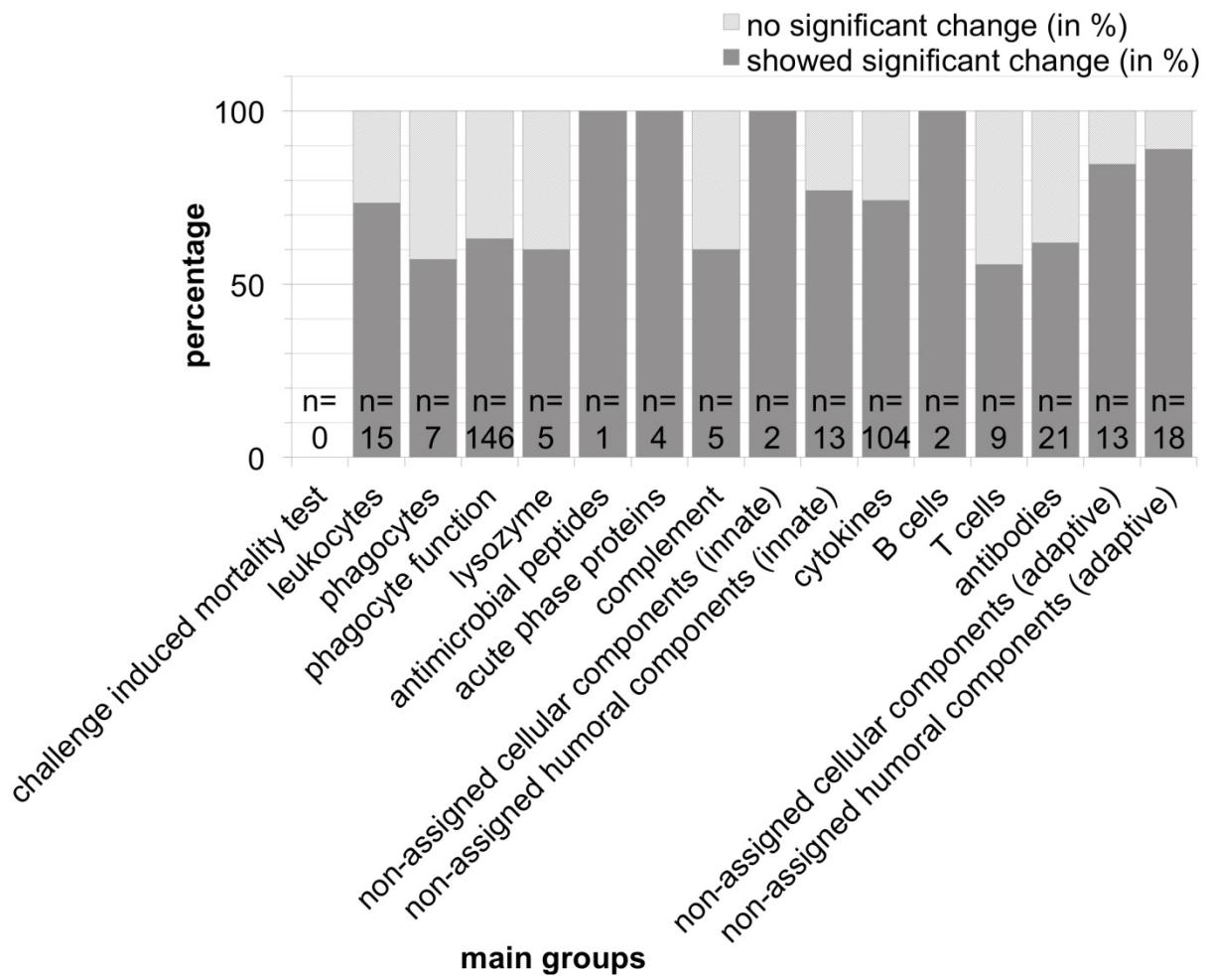


Fig 10