FURTHER DEVELOPMENT OF THE NCTC 2544 IL-18 ASSAY TO IDENTIFY CONTACT ALLERGENS

PREMIO FARMINDUSTRIA 2011

a Dott.ssa Valentina Galbiati

IPAM Roma, 19 ottobre 2011

Università degli Studi di Milano

PERCORSO FORMATIVO

- **Luglio 2010**: Laurea in Farmacia conseguita presso l'Università degli Studi di Milano, con tesi sperimentale svolta nel Laboratorio di Tossicologia del Prof. C.L. Galli (Dipartimento di Scienze Farmacologiche) sotto la guida della Prof.ssa Emanuela Corsini. Titolo della tesi: ***"Valutazione del potenziale allergenico di composti a basso peso molecolare basata sull'induzione selettiva di IL-18 in una linea di cheratinociti umani"***.
- **Dicembre 2010**: Esame di Stato. Abilitazione alla professione di farmacista.
- **Febbraio 2011**: vincitrice della selezione pubblica, per titoli ed esami, per il conferimento di una **borsa di studio per il proseguimento della formazione dei giovani più promettenti** di durata annuale, per l'area scientifico-disciplinare delle Scienze Farmaceutiche e Farmacologiche, presso il Dipartimento di Scienze Farmacologiche sotto la guida del Prof. Corrado Galli, con titolo *"Valutazione della potenza allergenica e determinazione della fototossicità attraverso metodi alternativi in vitro"* .

HYPERSENSITIVITY

ALLERGIC CONTACT DERMATITIS

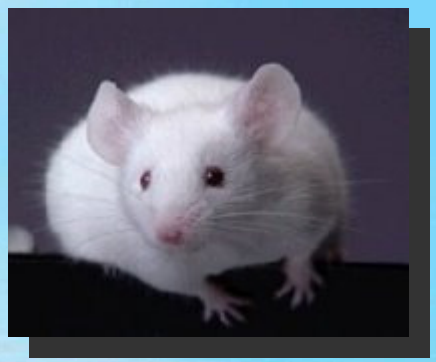
IS A FORM OF DELAYED TYPE HYPERSENSITIVITY REACTION AND AS SUCH IS DEPENDENT UPON CELL-MEDIATED IMMUNE RESPONSES AND THE ACTIVITY OF T CELLS

METHODS IN IMMUNOTOXICOLOGY

Hypersensitivity Testing

- ***Guinea Pig Tests***
  - *Maximization Test*
  - *Occlusive Patch Test*
  - Respiratory Challenge
  - Systemic Anaphylaxix

- ***Mouse Tests***
  - *Local lymph node assay (LLNA)*
  - Mouse Ear Swelling Test



SCENARIO LEGISLATIVO IN EU

- **7°Emendamento della Direttiva sui cosmetici (2003/15/CE)**

- **REACH (nuova legislazione delle sostanze chimiche)**

Esigenza di metodi alternativi validati in tutti campi dove sono richiesti studi di tossicità

KERATINOCYTES and IL-18

Toxicology in Vitro 23 (2009) 789–796

Contents lists available at ScienceDirect

Toxicology in Vitro

journal homepage: www.elsevier.com/locate/toxinvit

Use of IL-18 production in a human keratinocyte cell line to discriminate contact sensitizers from irritants and low molecular weight respiratory allergens

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Further development of the NCTC 2544 IL-18 assay to identify *in vitro* contact allergens

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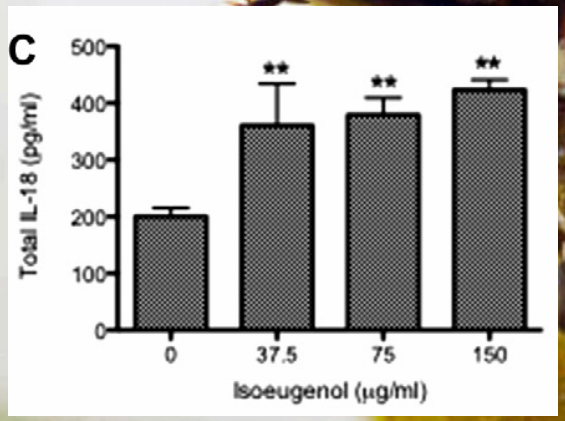
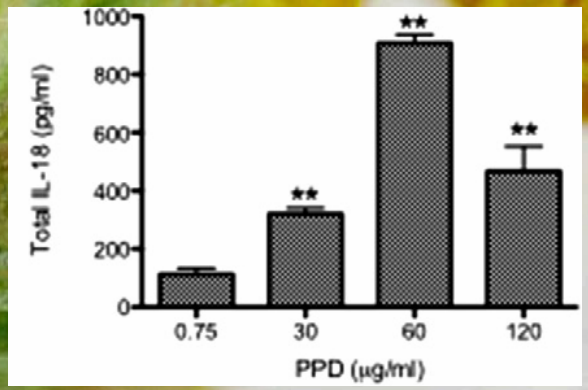
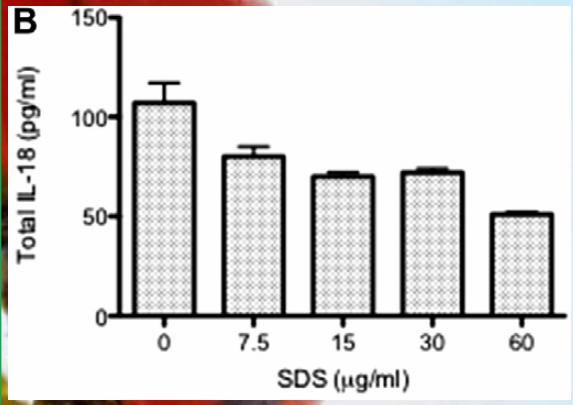
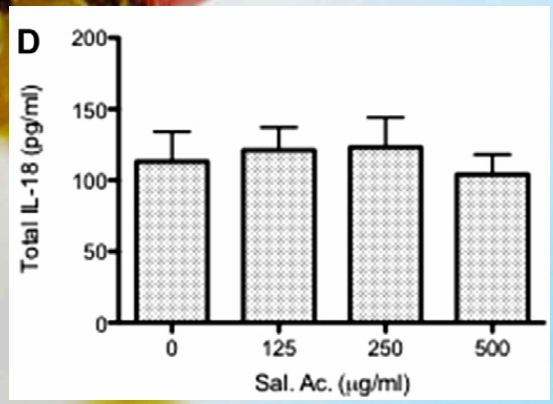
Contact allergens



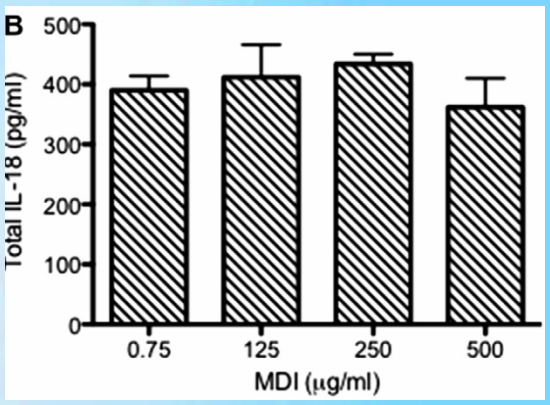


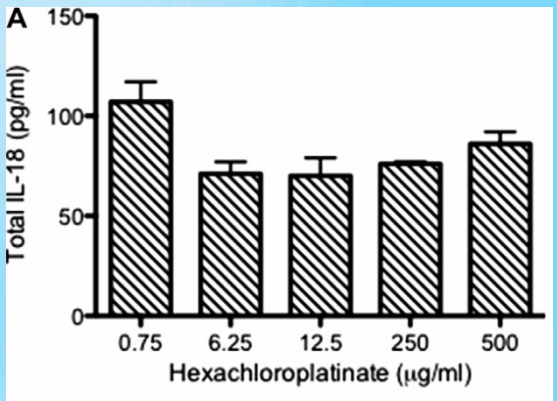
Irritants





Resp. allergens





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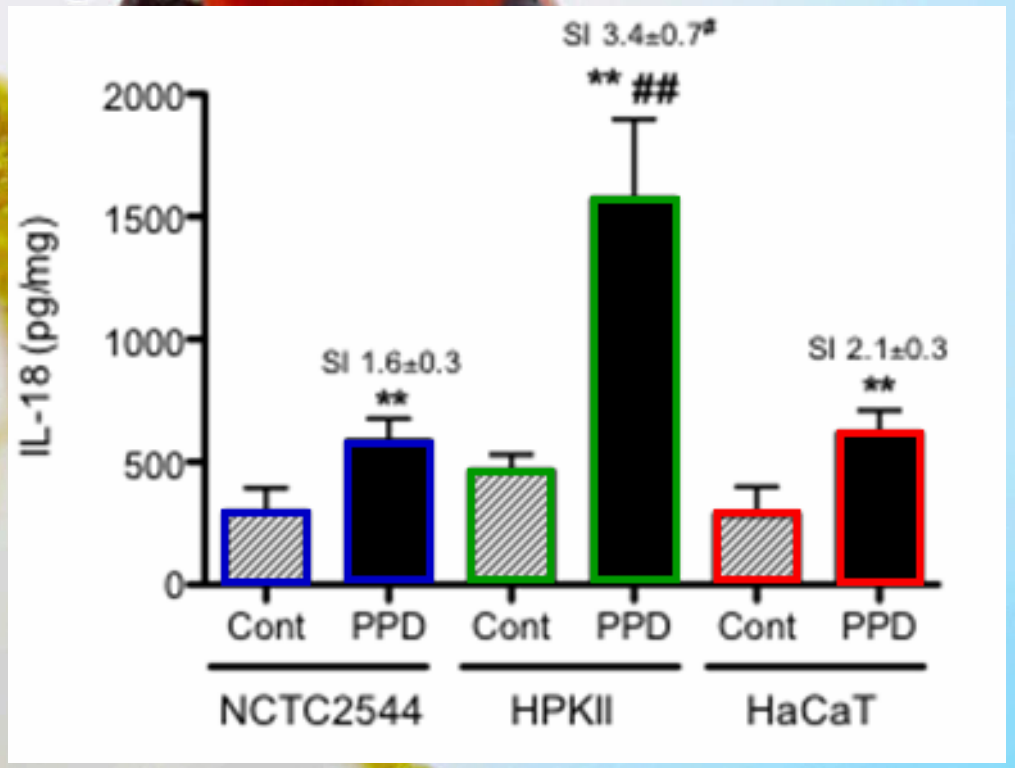
DIFFERENT HUMAN KC CELL LINES



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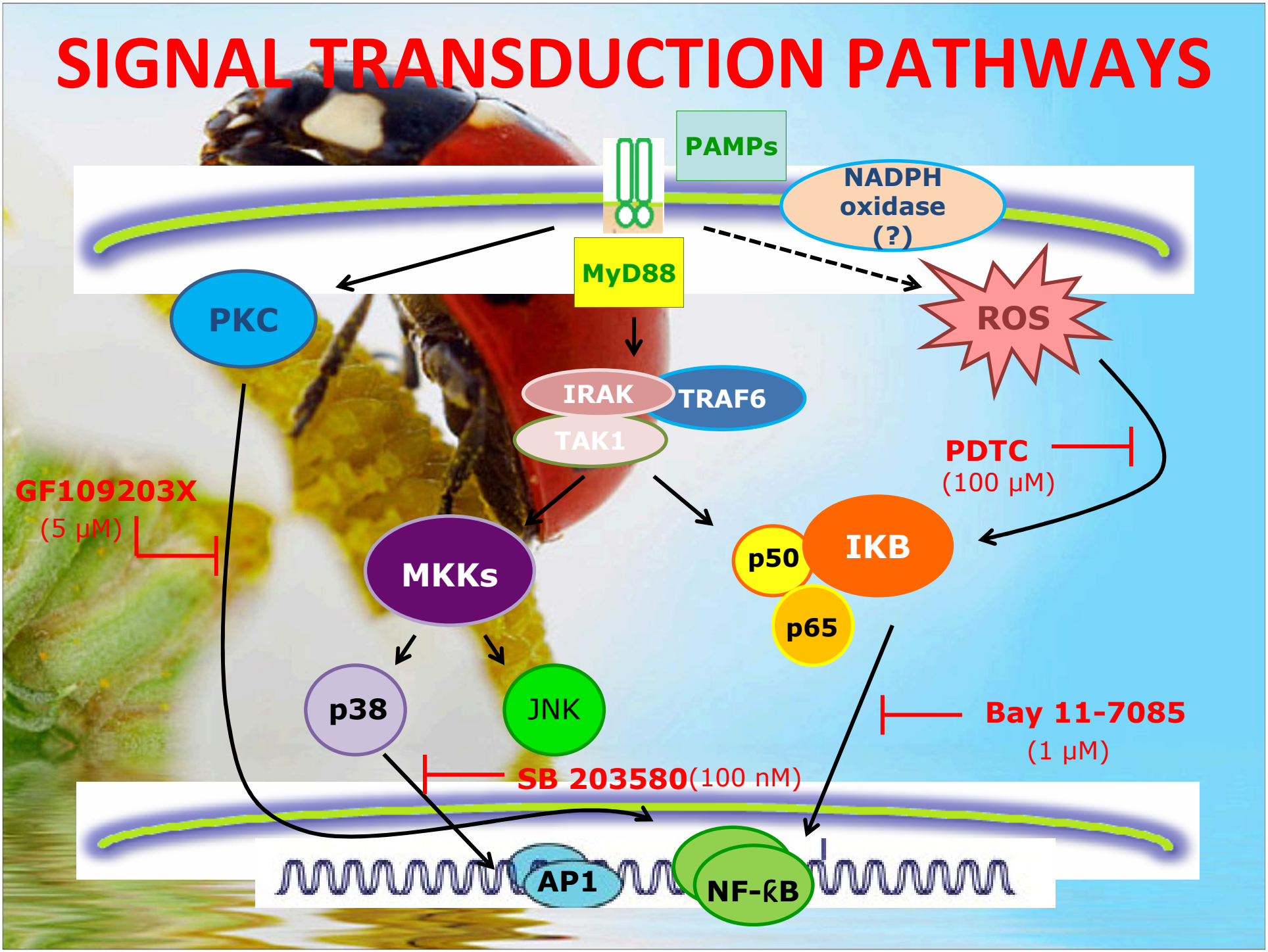
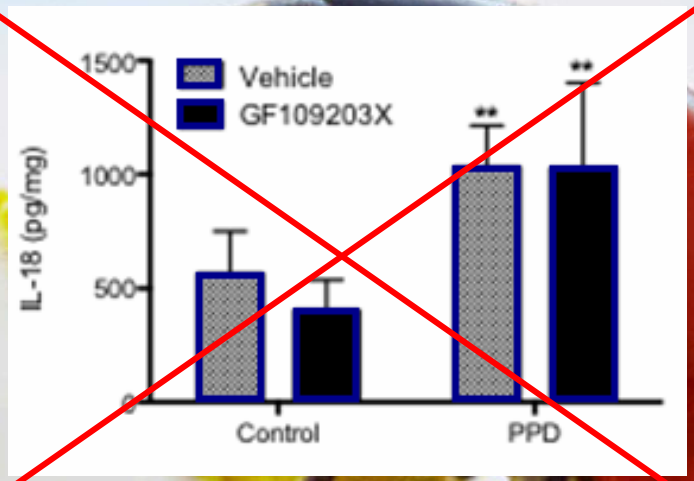
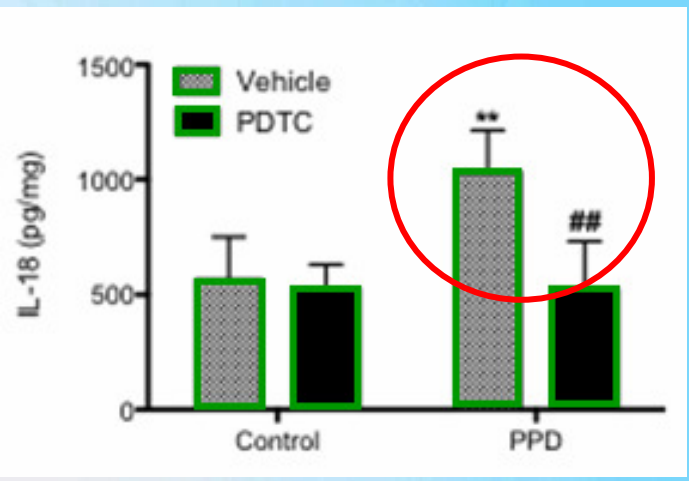

SIGNAL TRANSDUCTION PATHWAYS
PAMPs
NADPH oxidase (?)
MyD88
PKC
ROS
IRAK
TRAF6
TAK1
PDTC
(100 µM)
GF109203X
(5 µM)
MKKs
p50
IKB
p65
p38
JNK
Bay 11-7085
(1 µM)
SB 203580(100 nM)
AP1
NF-κB

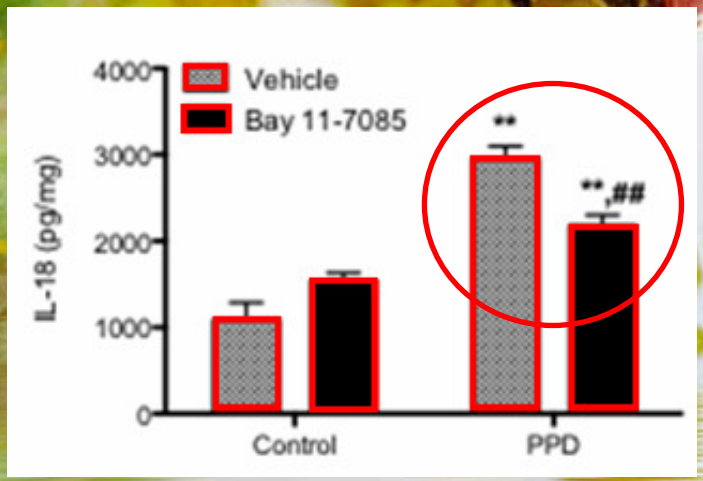
PKC



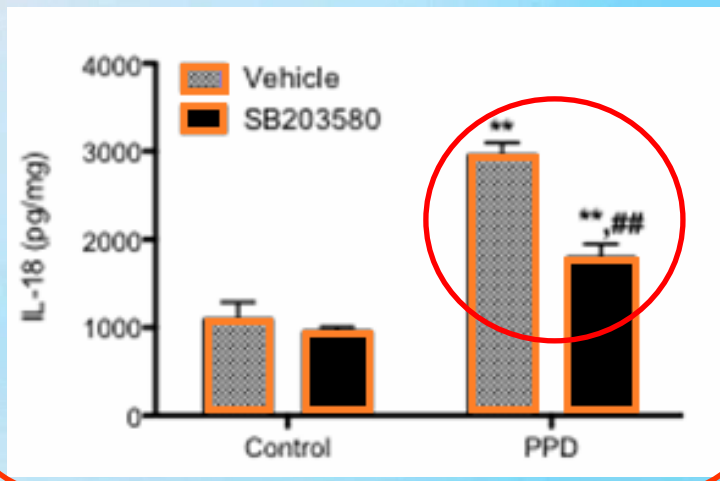
Oxidative stress



IκBα



p38 MAPK



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CONCLUSIONS

- ***Innate inflammatory reaction*** *has several important consequences for development of allergic contact dermatitis both in the induction and elicitation phases:*
  - activation and maturation of skin DC
  - DC migration to the draining lymph nodes
  - recruitment of DC precursors (i.e. blood monocytes)
  - T cells activation
- *Among the pro-inflammatory cytokines produced by KC, we demonstrated a selective increase in* ***IL-18****, which was observed only following treatment with contact allergens, whereas both irritants and respiratory allergens failed.*
- *Results obtained indicated a role for* ***oxidative stress,*** *NF-κB and p38 MAPK activation in PDD-induced IL-18 production.*

Ringraziamenti

Laboratorio Tossicologia

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Silvia Budello
Sara Bianchi

e…

Dott. Luca Tosti