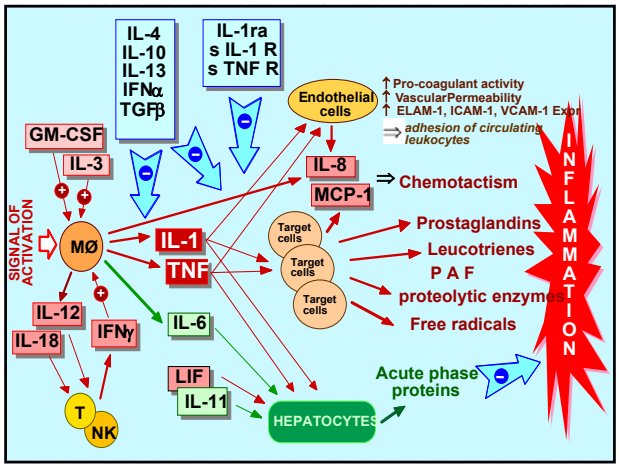
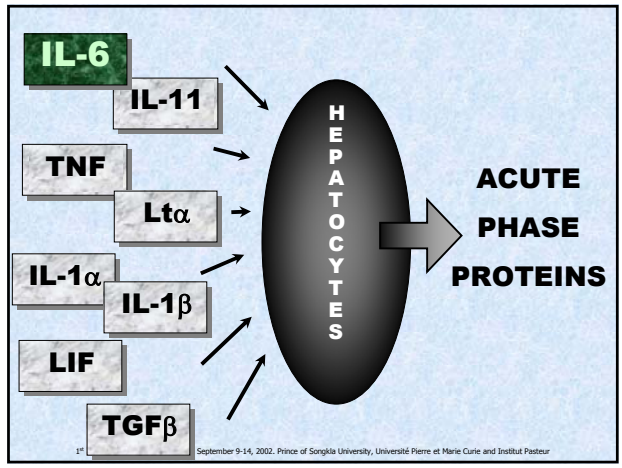
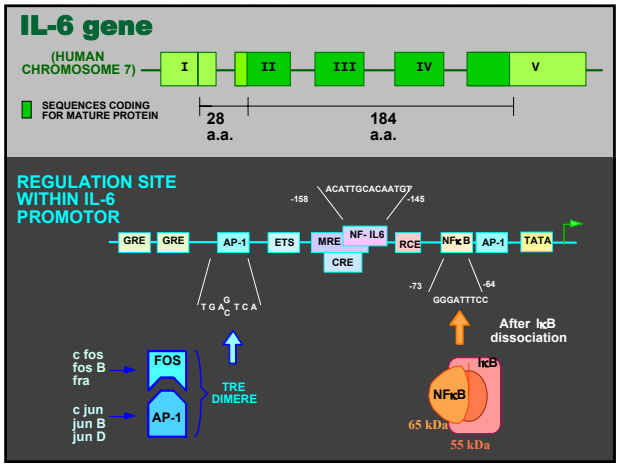
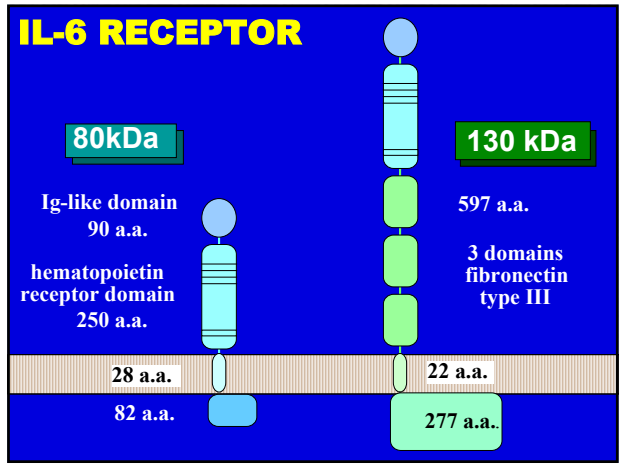
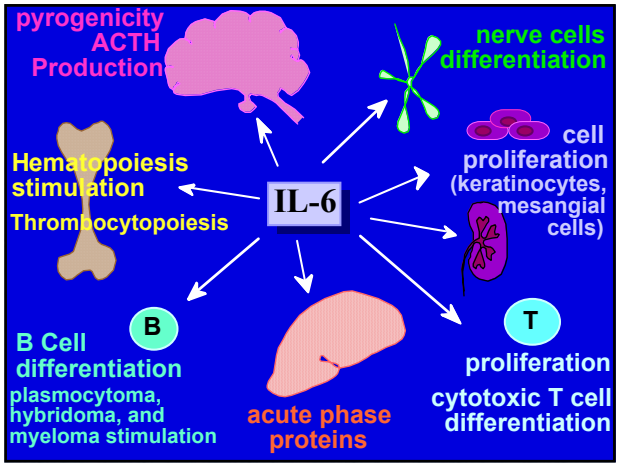
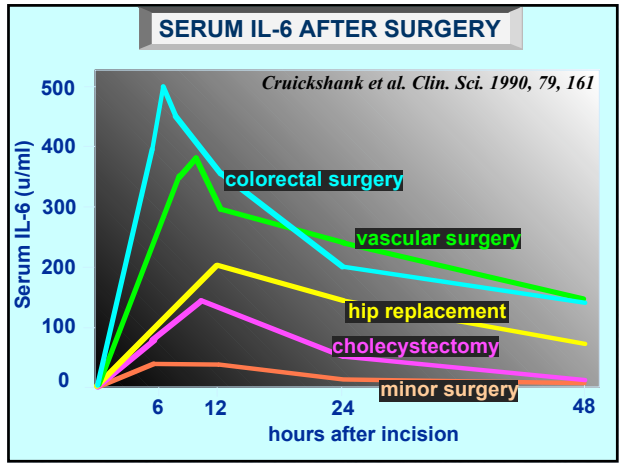

IL-4
IL-10
IL-13
IFNα
TGFβ
IL-1ra
s IL-1 R
s TNF R
Endothelial cells
↑Pro-coagulant activity
↑VascularPermeability
↑ELAM-1, ICAM-1, VCAM-1 Expr
⇒ adhesion of circulating leukocytes
GM-CSF
IL-3
IL-8
MCP-1
⇒ Chemotactism
SIGNAL OF ACTIVATION
MØ
IL-1
TNF
Target cells
Prostaglandins
Leucotrienes
P A F
proteolytic enzymes
Free radicals
IL-12
IFNγ
IL-18
IL-6
LIF
IL-11
Acute phase proteins
T
NK
HEPATOCYTES
INFLAMMATION


IL-6
IL-11
TNF
Lta
IL-1α
IL-1β
LIF
TGFβ
HEPATOCYTES
ACUTE PHASE PROTEINS
September 9-14, 2002. Prince of Songkla University, Université Pierre et Marie Curie and Institut Pasteur


IL-6 gene
(HUMAN CHROMOSOME 7)
I
II
III
IV
V
SEQUENCES CODING FOR MATURE PROTEIN
28 a.a.
184 a.a.
REGULATION SITE WITHIN IL-6 PROMOTOR
ACATTGCACAATGT
-158
-145
GRE
GRE
AP-1
ETS
MRE
NF- IL6
CRE
RCE
NFκB
AP-1
TATA
-73
-64
GGGATTTCC
TGAGTCA
After IκB dissociation
c fos
fos B
fra
c jun
jun B
jun D
FOS
AP-1
TRE DIMERE
IκB
NFκB
65 kDa
55 kDa


IL-6 RECEPTOR
80kDa
Ig-like domain 90 a.a.
hematopoietin receptor domain 250 a.a.
130 kDa
597 a.a.
3 domains fibronectin type III
28 a.a.
82 a.a.
22 a.a.
277 a.a.


pyrogenicity
ACTH
Production
nerve cells differentiation
Hematopoiesis stimulation
Thrombocytopoiesis
IL-6
cell proliferation (keratinocytes, mesangial cells)
B
B Cell differentiation
plasmocytoma, hybridoma, and myeloma stimulation
acute phase proteins
T
proliferation
cytotoxic T cell differentiation


SERUM IL-6 AFTER SURGERY
Cruickshank et al. Clin. Sci. 1990, 79, 161
Serum IL-6 (u/ml)
500
400
300
200
100
0
colorectal surgery
vascular surgery
hip replacement
cholecystectomy
minor surgery
6
12
24
48
hours after incision

CIRCULATING CYTOKINES AND BOWEL INFLAMMATORY DISEASES

		IL-6 n	IL-6 percent above detection limit (> 4 pg/ml)	IL-8 n	IL-8 percent above detection limit (> 20pg/ml)
Control		61	10%	20	10%
Crohn's disease	active	20	90%	21	38%
	inactive	9	22%	28	18%
Ulcerative colitis	active	34	41%	23	43%
	inactive	13	8%	25	16%
		Mitsuyama et al. 1991 Gastroenterol. jpn 26, 20		*Jones et al. 1993 J.Gastroenterol. Hepatol. 8, 508*	

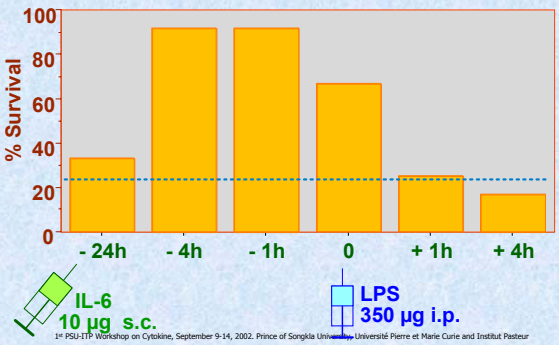
SYSTEMIC IL-6 DETECTION IN RESPONSE TO A LOCALIZED INFLAMMATION

Kimber et al. Int. Arch. All. Appl. Immunol. 1990, 92, 97

	T0	+ 24h
Ear thickness	0	+ 80 %
Plasma IL-6	< 50 pg/ml	600 pg/ml

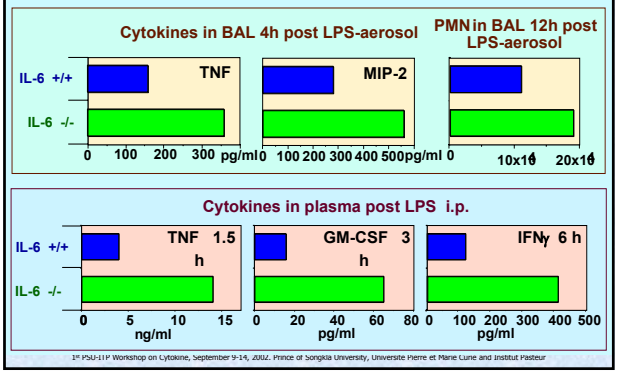
INJECTION TIME OF IL-6 DETERMINE FATAL OUTCOME IN EXPERIMENTAL ENDOTOXIN SHOCK

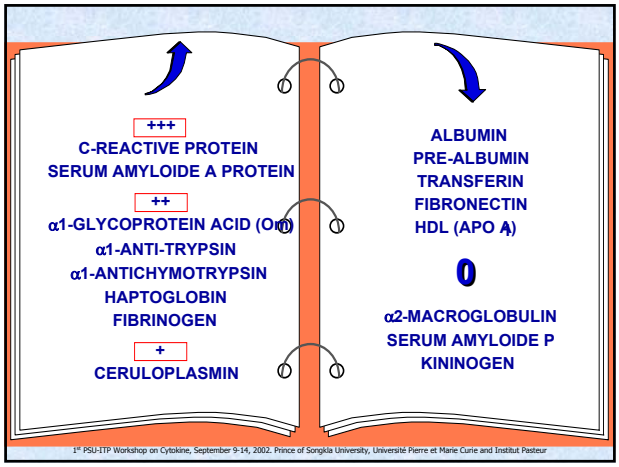
Yoshizawa et al. J Interferon Cytokine Res. 1996, 16, 995



IL-6 IS AN ANTI-INFLAMMATORY CYTOKINE REQUIRED FOR CONTROLLING LOCAL OR SYSTEMIC ACUTE INFLAMMATORY RESPO

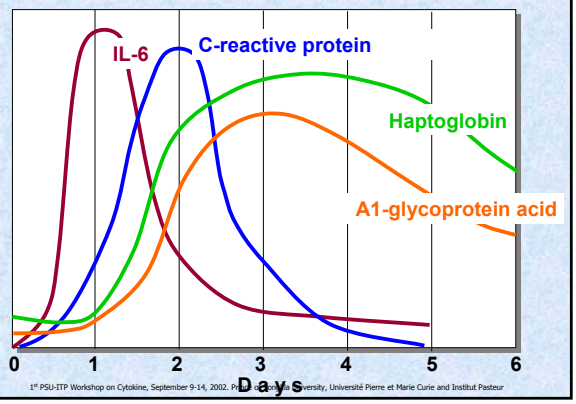
Xing et al. J Clin Invest 1998, 101, 311



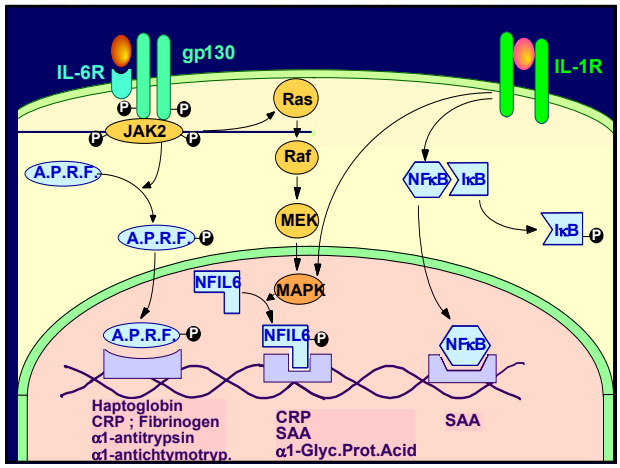


KINETICS OF IL-6 AND MAIN ACUTE PHASE PROTEINS

After an inflammatory insult on day 0



	Human	rat	mouse	rabbit
C R P	+++	+	0	+++
S A A	+++	X	+++	?
α1-Glyc.Prot.Ac.	++	++	+	++
Haptoglobin	++	++	++	+
α2-macroglobulin	0	+++	0	0
S A P	0	0	+++	0
α1-Acute Phase	X	+++	X	X



FUNCTIONS OF ACUTE PHASE PROTEIN

ELIMINATION

CRP + POLYSACCHARIDIC or PHOSPHOLIPIDIC LIGANDS
ex. Chromatin ; damaged membran
(via phosphorylcholin or galactose motifs)

Ca^{++}

CRP / LIGAND / C1q → C3 CONVERTASE

CRP / LIGAND / C3b → C3a + C3b + C3

OPSONISATION

FUNCTIONS OF ACUTE PHASE PROTEIN

ELIMINATION

HAPTOGLOBIN + HEMOGLOBIN → PHAGOCYTOSIS

CÉRULOPLASMIN + 0_2^- + 2 H^+ → $H_2O_2 + O_2$

FUNCTIONS OF ACUTE PHASE PROTEINS

ANTI-PROTEASES

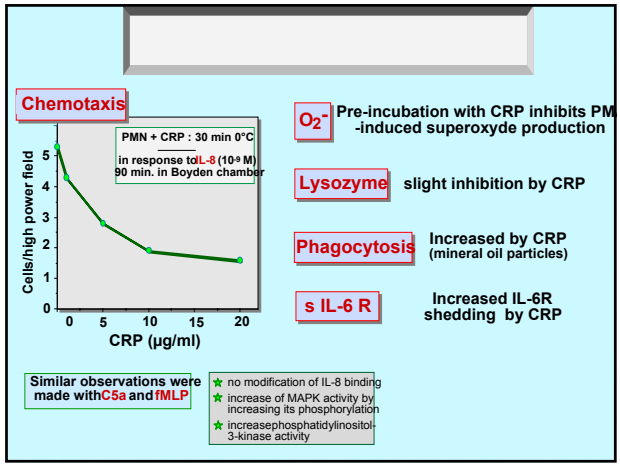
α1-ANTI-TRYPSIN + ELASTASE → [α1-ANTI-TRYPSIN / ELASTASE]

α1-ANTICHYMOTRYPSIN CATHEPSIN-G → [α1-ANTICHYMOTRYPSIN CATHEPSIN-G]

\+ α2-MACROGLOBULIN → [α2-MACROGLOBULIN ELASTASE]

[α2-MACROGLOBULIN CATHEPSIN-G]

PHAGOCYTOSIS

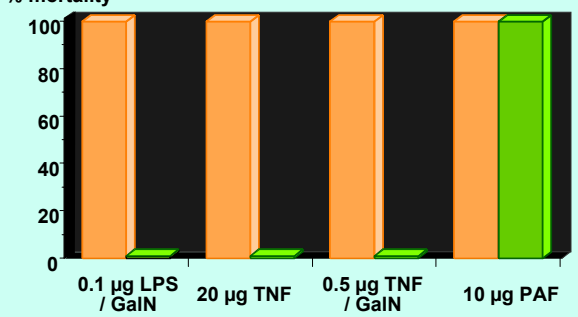


PBS

+ α1-Anti-Trypsin (T - 2h : 1 mg i.p.)

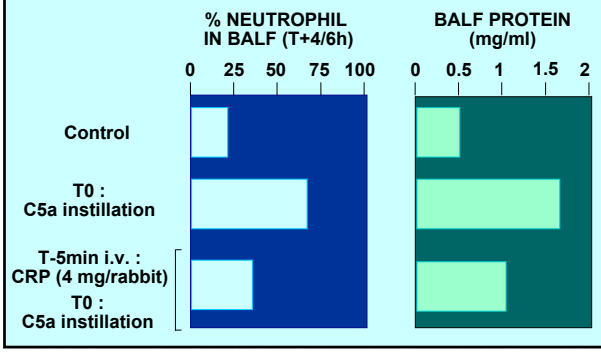
α1-anti-trypsin inhibits the lethal response to TNF in mice

Libert et al. J.Immunol. 1996, 157, 5126



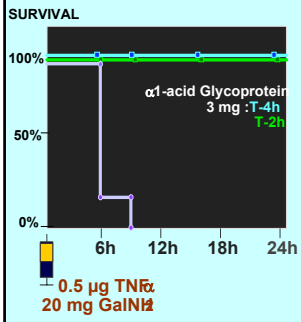
ANTI-INFLAMMATORY PROPERTIES OF CRP

Heuertz et al. Am.J.Pathol. 1993,142, 319



Protection by α1-acid glycoprotein against TNF-induced lethality

Libert et al. J.Exp.Med. 1994,180,1571



T-2h	challenge	Survival
-	20 µg TNFα	0/8
αAGP	"	5/5
-	0.1 µg LPS+GalNH2	0/5
αAGP		5/5

IL-6 INDUCES IL-1Ra AND s TNF R IN HUMANS

Tilg et al. Blood 1994, 83, 113

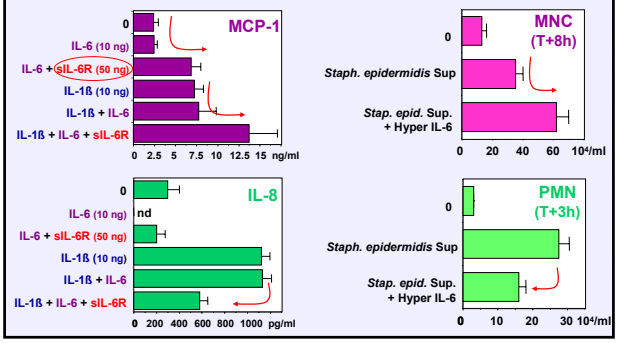
	IL-6	IL-1Ra	s p55 TNF R
120 h INFUSION IN CANCER PATIENTS		Peak : 2-4 h 9.6 ± 1.7 ng/ml back to baseline at 24h baseline 0.4 ng/ml (*vs* 0.4 in healthy subjects)	Increase within 4-8h and continuous increase up to 12.2 ng/ml baseline 3.2 ng/ml (*vs* 1.4 in healthy subjects)
PMBC		production of a small amount no synergy with LPS	below detection limit
Mo + GM-CSF for 6 days		more responsive than fresly isolated Mo	

IL-6 & sIL-6R orchestrate the switch of leukocyte recruitment during inflammation

Hurst et al. Immunity 2001, 14, 705

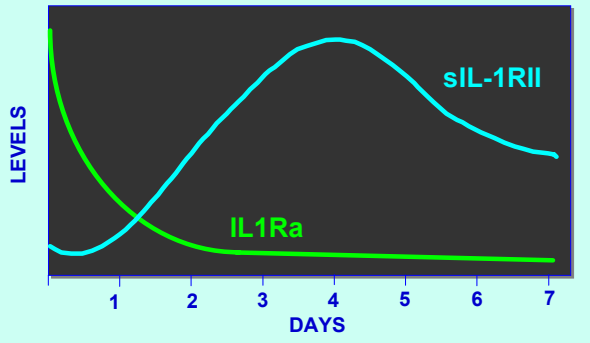
Chemokine production by human mesothelial cells

Cellular recruitment in peritoneal cavity of IL-6 -/- mice

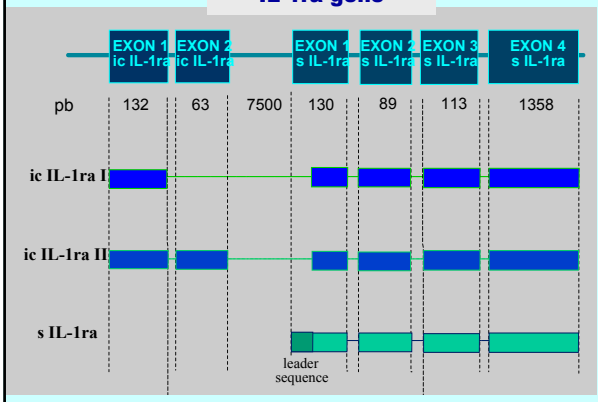


TIME COURSE OF IL-1Ra and sIL-1RII IN PATIENTS WITH MENINGOCOCCAL MENINGITIDIS

van Deuren et al. Blood 1997, 90, 1101



IL-1ra gene



INTESTINAL IL-1ra PRODUCTION

Cominelli et al. J.Biol.Chem. 1994, 269,6962

IL-1ra IN NORMAL AND INFLAMED RABBIT COLONIC TISSUE (ng/g colon)

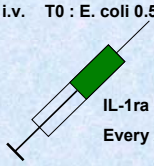
	Healthy rabbits	Colitis *	Colitis + corticosteroids
IL-1α	< 0.4	20 ± 4	12 ± 3
IL-1ra	49 ± 6	150 ± 40	148 ± 33

* T0 formaldehyde in the colon
T+2h BSA - Anti-BSA i.v.

INTERLEUKIN-1 RECEPTOR ANTAGONIST REDUCES MORTALITY FROM ENDOTOXIN SHOCK

Ohlson et al. Nature 1990, 348, 550

i.v. T0 : E. coli 0.5 mg/kg +/- IL-1ra



IL-1ra (100 mg/kg)
Every 2 h for 24 h

SURVIVAL ON DAY 7

Saline : 20 %

IL-1ra : 90 %

Improvement :
Mean arterial pressure
White blood cell counts
Cellular infiltrate in the lungs

Confirmed in mice by :
Wakabayashi et al. FASEB J. 1991, 5, 338
Alexander et al. J. Exp. Med. 1991, 173, 1029

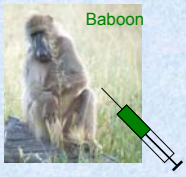
IL-1ra improves survival and hemodynamic performance in E. coli septic shock

Fischer et al. J. Clin. Invest. 1992, 89, 1551

Baboons	Sublethal endotoxemia	E. coli septic shock
mean arterial pressure	n.s.	improvement *
cardiac output	n.s.	improvement
heart rate	n.s.	n.s.
Leukopenia	n.s.	n.s.
Survival (24 h)	-	7/7 vs 3/7
TNF	n.s.	n.s.
IL-1	-	decrease
IL-6	n.s.	decrease
IL-8	n.s.	n.s.

* < fluid resuscitation

PROTECTION INDUCED BY SOLUBLE TNF RECEPTOR



Van Zee et al. PNAS 1992, 89, 4845

T0 : *E.coli* [LD 100]
Infusion = 30 min

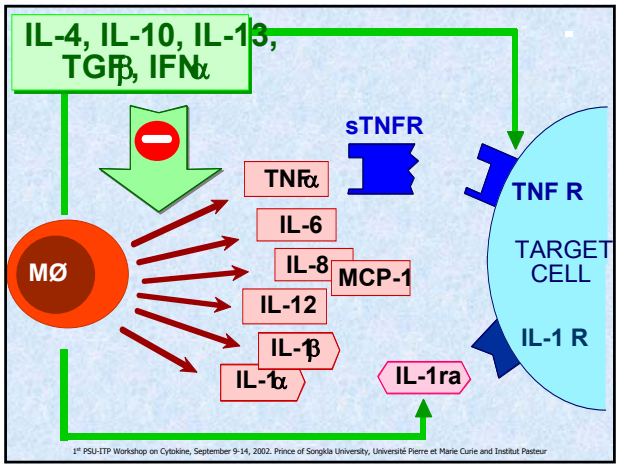
T0 : ± s TNF R
(molar excess x 300)
Infusion = 3 h

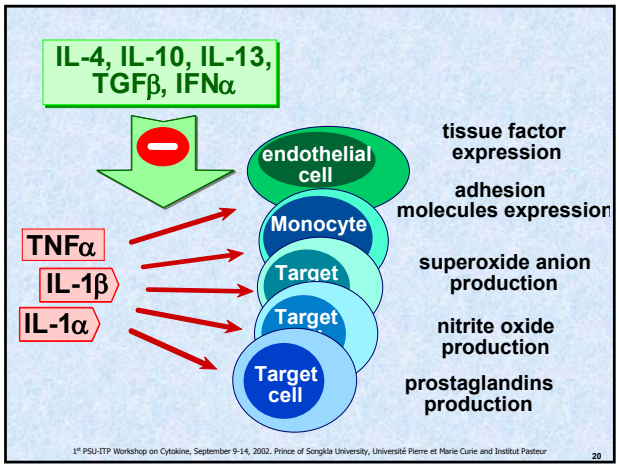
	E. coli	*E. coli* + S TNF R I
TNF (2h)	30 ng/ml	< d.l.
IL-1β (3h)	2.5 ng/ml	0.5 ng/ml
IL-6 (8 h)	20 000 u/ml	9 000 u/ml
Mean arterial pressure	- 56 %	- 29 %
Resuscitation fluid required to maintain hemodynamic stability	163 ml/kg	13 ml/kg

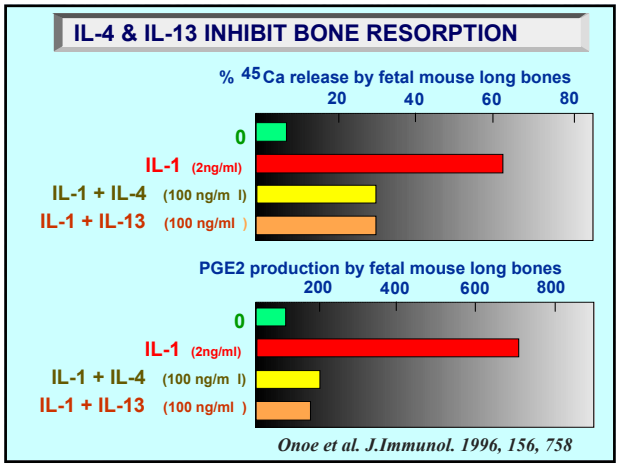
CIRCULATING TNF & sTNFR IN SEVERE MENINGOCOCCAEMIA

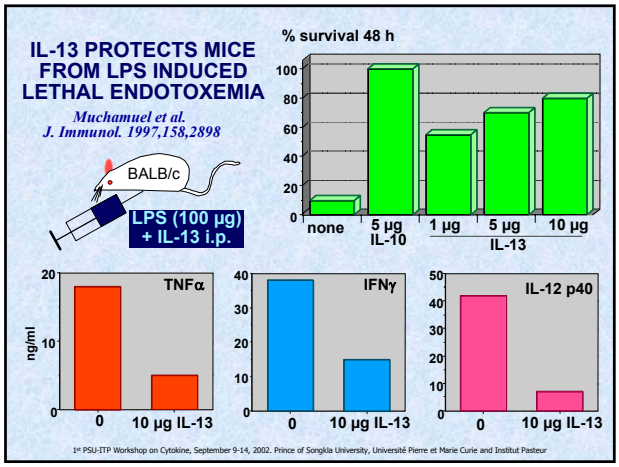
Girardin et al. Immunol. 1992, 76, 20

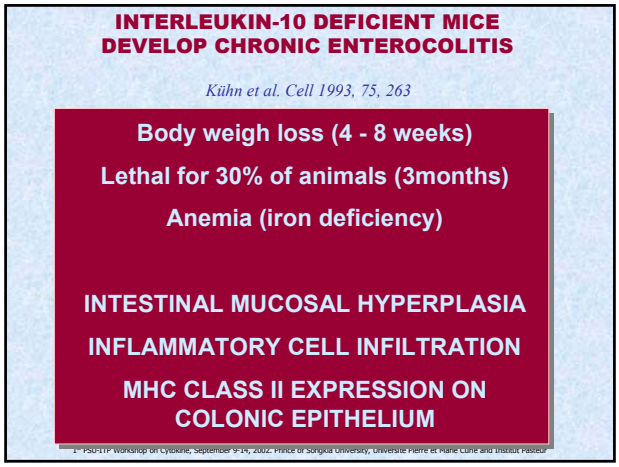
ON ADMISSION	*SURVIVALS* n = 26	*DEATH* n = 9	*p*
TNF	470 pg/ml	1466 pg/ml	0.001
s TNF R I	26.3 ng/ml	35.4 ng/ml	0.007
S TNF R II	67.8 ng/ml	93.3 ng/ml	0.04

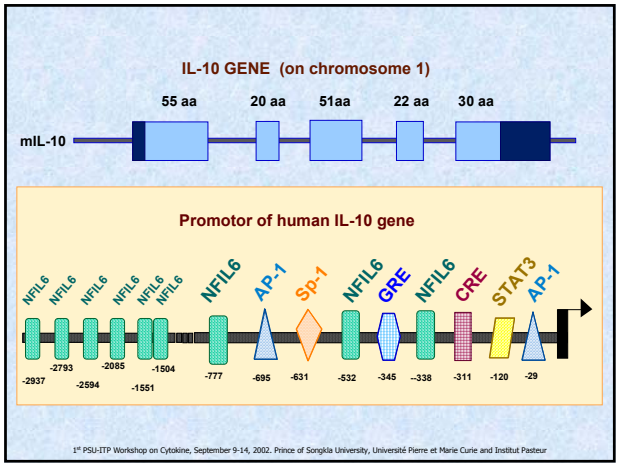

IL-4, IL-10, IL-13, TGFβ, IFNα
sTNFR
TNFα
IL-6
IL-8
MCP-1
IL-12
IL-1β
IL-1α
MØ
TNF R
TARGET CELL
IL-1 R
IL-1ra


IL-4, IL-10, IL-13, TGFβ, IFNα
TNFα
IL-1β
IL-1α
endothelial cell
Monocyte
Target
Target
Target cell
tissue factor expression
adhesion molecules expression
superoxide anion production
nitrite oxide production
prostaglandins production

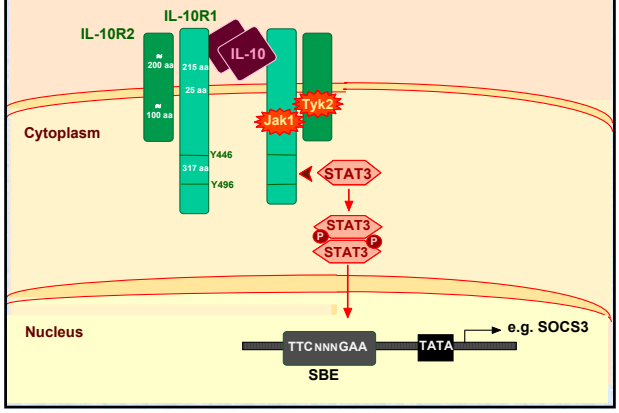

IL-4 & IL-13 INHIBIT BONE RESORPTION
% 45Ca release by fetal mouse long bones
20
40
60
80
0
IL-1 (2ng/ml)
IL-1 + IL-4 (100 ng/m l)
IL-1 + IL-13 (100 ng/ml)
PGE2 production by fetal mouse long bones
200
400
600
800
0
IL-1 (2ng/ml)
IL-1 + IL-4 (100 ng/m l)
IL-1 + IL-13 (100 ng/ml)
Onoe et al. J.Immunol. 1996, 156, 758


IL-13 PROTECTS MICE FROM LPS INDUCED LETHAL ENDOTOXEMIA
Muchamuel et al.
J. Immunol. 1997,158,2898
BALB/c
LPS (100 µg) + IL-13 i.p.
% survival 48 h
100
80
60
40
20
0
none
5 µg IL-10
1 µg
5 µg
10 µg
IL-13
ng/ml
TNFα
IFNγ
IL-12 p40
0
10 µg IL-13


INTERLEUKIN-10 DEFICIENT MICE DEVELOP CHRONIC ENTEROCOLITIS
Kühn et al. Cell 1993, 75, 263
Body weigh loss (4 - 8 weeks)
Lethal for 30% of animals (3months)
Anemia (iron deficiency)
INTESTINAL MUCOSAL HYPERPLASIA
INFLAMMATORY CELL INFILTRATION
MHC CLASS II EXPRESSION ON COLONIC EPITHELIUM

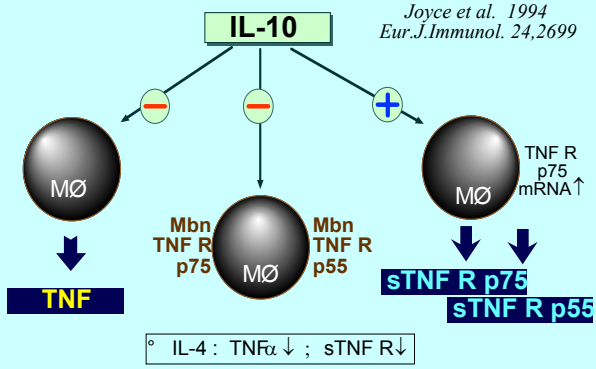

IL-10 GENE (on chromosome 1)
55 aa
20 aa
51aa
22 aa
30 aa
mIL-10
Promotor of human IL-10 gene
NFIL6
AP-1
Sp-1
GRE
CRE
STAT3
-2937
-2793
-2594
-2085
-1551
-1504
-777
-695
-631
-532
-345
-338
-311
-120
-29

IL-10 RECEPTOR AND SIGNAL TRANSDUCTION PATHWAY



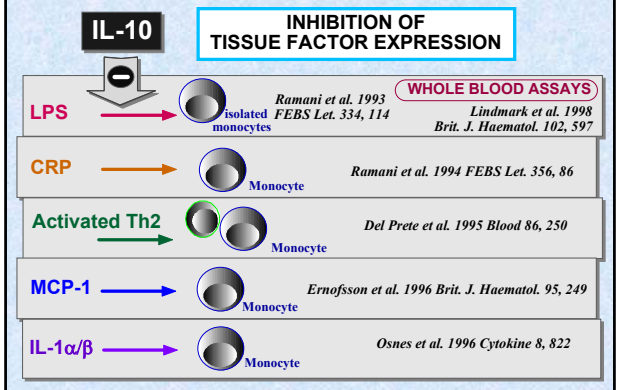
IL-10 REDUCES THE PRO-INFLAMMATORY POTENTIAL OF TNF IN 3 WAYS

Joyce et al. 1994 Eur.J.Immunol. 24,2699



° IL-4 : TNFα ↓ ; sTNF R↓

IL-10 INHIBITION OF TISSUE FACTOR EXPRESSION



1st PSU-ITP Workshop on Cytokine, September 9-14, 2002. Prince of Songkla University, Université Pierre et Marie Curie and Institut Pasteur

PROTECTIVE EFFECTS OF IL-4 AND IL-10 AGAINS IMMUNE COMPLEX-INDUCED LUNG INJURY

Mulligan et al. J. Immunol. 1993, 151, 5666

i.v. : Intratracheally :	BSA Anti-BSA	BSA Anti-BSA + IL-4	BSA Anti-BSA + IL-10
Permeability index	1.0	0.57	0.56
Hemorrhage index	0.22	0.12	0.11
BALneutrophils (x10⁶)	26	12	11
BAL TNFα (units)	287	63	67
ICAM-1 expression (cpm x 10³)	4200	2700	2700

IL-10 IN IgG IMMUNE COMPLEX-INDUCED LUNG INJURY

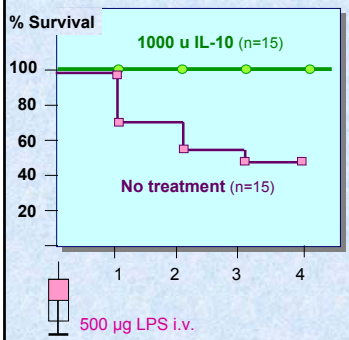
Shanley et al. J. Immunol. 1995,154,3454

	T0	PEAK EXPRESSION
IL-10 mRNA	±	T = 4h +++++
IL-10	6.2 ng /mg lung	T = 2h : 14 ng /mg lung

T0 i.v.	Permeability index (^{125}I-albumine leakage)		TNFα in BAL (pg/ml)	
none	0.57 ± 0.04		1678 ± 262	
Control serum	0.52 ± 0.05	*p<0.001*	1794 ±359	*p<0.001*
anti-IL-10	0.85 ± 0.05		2981 ± 249	

IL-10 REDUCES THE RELEASE OF TNF AND PREVENTS LETHALITY IN EXPERIMENTAL ENDOTOXEMIA

Gérard et al . J. Exp. Med. 1993, 177, 547



Challenge 500 µg LPS
n = 5 in each group

Pre-treatment (-30 min; i.p.)	TNF serum level (1.5 h)
Medium	5268 pg
IL-10 (10 U)	1216 pg
IL-10 (1000 U)	416 pg

1st PSU-ITP Workshop on Cytokine, September 9-14, 2002. Prince of Songkla University, Université Pierre et Marie Curie and Institut Pasteur

IL-10 AND IMMUNE DEPRESSION

HUMAN SEPTIC SHOCK	Brandzaeg et al. *J. Exp. Med.* 1996, 184, 51 Randow et al. *J. Exp. Med.* 1995, 181, 1887
SEPSIS-INDUCED IMPAIRMENT IN LUNG ANTIBACTERIAL HOST DEFENSE	Steinhauser et al. *J. Immunol.* 1999, 162, 392
MØ DEACTIVATION IN SEPTIC PERITONITIS	Reddy et al. *Infect. Immun.* 2001, 69, 1394
BURN INJURY	Lyons et al. *Arch Surg.* 1999, 134, 1317
TUBERCULOSIS ASSOCIATED ANERGY	Boussiotis et al. *J. Clin. Invest.* 2000, 105, 1317
KALA AZAR (Leishmania chagasi)	Holaday et al. *J. Clin. Invest.* 1993, 92, 2626
Ag-SPECIFIC HYPORESPONSIVENESS IN HUMAN LYMPHATIC FILARIASIS	Mahanty et al. *J. Infect. Dis.* 1996, 173, 769
PARASITE-SPECIFIC ANERGY IN HUMAN URINARY SHISTOSOMIASIS	King et al. *J. Immunol.* 1996, 156, 4715

IL-10 AND DISEASES

BENEFICIAL

LETHAL ENDOTOXEMIA	Howard et al. *J. Exp. Med.* 1993, 177, 1205
RHEUMATOID ARTHRITIS	van Roon et al. *Arth.Rheum.* 1996; Persson et al. *Scand.J.Immunol. 1996*
PSORIASIS	Asadullah et al.J. Clin. Invest. 1998, 101, 783
THROMBOSIS	Downing et al. *J. Immunol.* 1998, 161, 1471
CONTACT HYPERSENSITIVITY	Ferguson et al. *J. Exp. Med.* 1994, 179, 1597
Ag-INDUCED AIRWAY INFLAMMATION	Zuany-Amorim et al. *J. Clin. Invest.* 1995, 95, 2644
IMMUNE COMPLEX-INDUCED LUNG INJURY	Mulligan et al. *J. Immunol.* 1993, 151, 5666
ISCHEMIA-REPERFUSION INJURY	Daemen et al. *Transplantation* 1999, 67, 792
CROHN'S DISEASE	Schreiber et al.; Fedorak et al. *Gastroenterol.* 2000, 119, 1461 & 1473

DELETERIOUS

AUTOIMMUNE DIABETES	Ishida et al. *J.Exp.Med* 1994; Lee et al. *J.Exp.Med.* 1996
LUPUS ERYTHEMATOSUS	Llorente et al. *Arthr. Rheum.* 2000, 43, 1790
BONE MARROW GRAFT	Blazar et al. *Blood* 1995, 85, 842
HEART & LIVER TRANSPLANT	Qian et al. *Transplantation* 1996; Li et al. *Transplantation* 1998
ENDOTOXIN-INDUCED UVEITIS	Rosembaum et al. *J. Immunol.* 1995, 155, 4090
ALLOGRAFT ARTERIAL DISEASE	Furukawa et al. *Am. J. Pathol.* 1999, 155, 1929

TGFβ1 KO mice

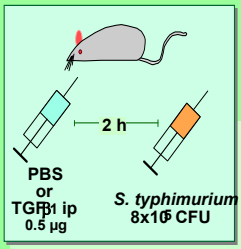
MULTIFOCAL INFLAMMATORY DISEASE

Shull et al. Nature 1992,359,693

Age at death	24 days
Site of inflammation cell infiltration / necrosis	stomach / Liver / pancreas / myocardium & endocardium / striated muscle / serosa
blood leukocytes	increased number of monocytes and immature neutrophils

PCR analysis of cytokines (spleen, liver, lung)

	TGFβ1	IFNγ	TNFα	MIP-1α	IL-1β	
Normal	+	-	-	-	+	
TGFβ1 KO	-	+	+	+	+	(++ in liver)



EFFECT OF TGFβ ON *S. typhimurium* INFECTION

Galdiero et al. Infect. Immun. 1999, 67, 1432

	DAY 5 PBS	DAY 5 TGFβ1
SURVIVAL	6/10	10/10
CFU / Spleen (log)	22	15
µM NO_2 production by splenic MØ	5	20
IL-1α production by LPS-activated spleen cells	800	1400
IFNγ production by LPS-activated spleen cells	1150	1800
IL-10, IFNγ iNOS mRNA expression in spleen		↗

IN VIVO EFFECT OF TGFβ ON LPS-INDUCED HYPOTENSION & LETHALITY

Perrella et al. PNAS 1996, 93, 2054

i.v.

S. typhosa LPS 4 mg/kg

TGFβ (20 µg/kg) + 200 ng/kg/min infusion

	Mean arterial pressure 120 min (mm Hg)	Survival 150 min.
0	110	100%
LPS	40	35%
LPS + TGFβ	100	90%

i.p.

S. typhosa LPS (4 mg/kg)

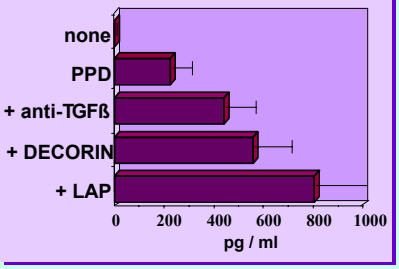
TGFβ 20 µg/kg

iNOS mRNA	Heart	Kidney	Liver	Lung
LPS			100%	
LPS + TGFβ	37%	20%	10%	50%

NATURAL INHIBITORS OF TGFβ

Hirsch et al. PNAS 1997, 94, 3926

IFNγ production by PBMC from tuberculosis patients



PRECURSOR FORM

LAP = LATENCY ASSOCIATED PROTEIN

MATURE TGFβ

DECORIN = 45 kDa proteoglycan abundant in extracellular matrix

WOUND HEALING

After inflammation TGFβ plays a critical role in resolution of the response, tissue repair and fibrosis

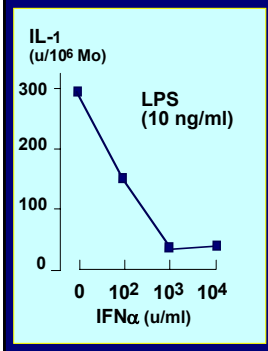
-The response initiated by TGFβ is self limited and reversible (short half life; TGFβ R)
- TGFβ cannot prevent leukocyte programmed cell death

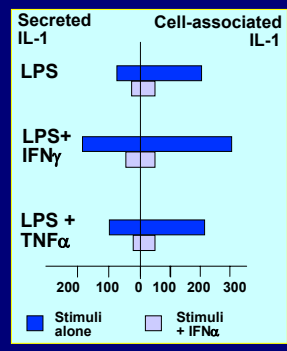
TGFβ regulates
- angiogenesis
- chemotaxis
- fibroblast proliferation
- synthesis and degradation of extra-cellular matrix

TGFβ → Fibroblast → collagen , fibronectin glycosaminoglycan

INHIBITION OF HUMAN MONOCYTE IL-1 PRODUCTION BY INTERFERON ALPHA

DANIS et al. Clin. Exp. Immunol. 1990, 80, 435





ANTI-INFLAMMATORY PROPERTIES OF INTERFERON ALPHA

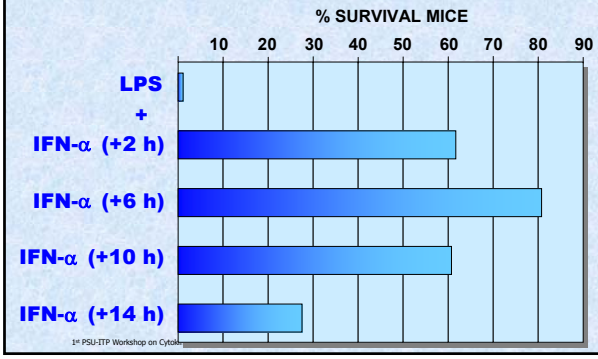
Tilg et al. Blood 1995,85,433

In vivo (in humans) s TNF R p55	
none	1.0 - 1.5 ng/ml
IFNα 5x106 U T + 12h	3.8 ± 0.4 ng/ml

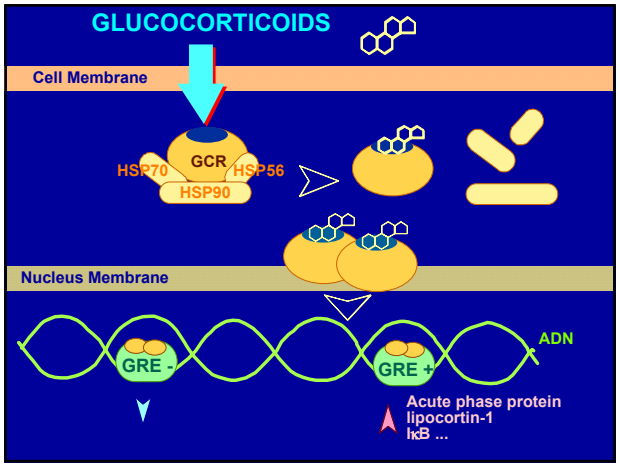
in vitro PBMC TNFα (ng/ml)	
IL-1α (100 ng/ml)	3.2 ± 0.3
+ IFNα 10 U/ml	2.5 ± 0.2
100 U/ml	1.4 ± 0.2

INTERFERON-α PREVENTS ENDOTOXIN INDUCED MORTALITY IN MICE

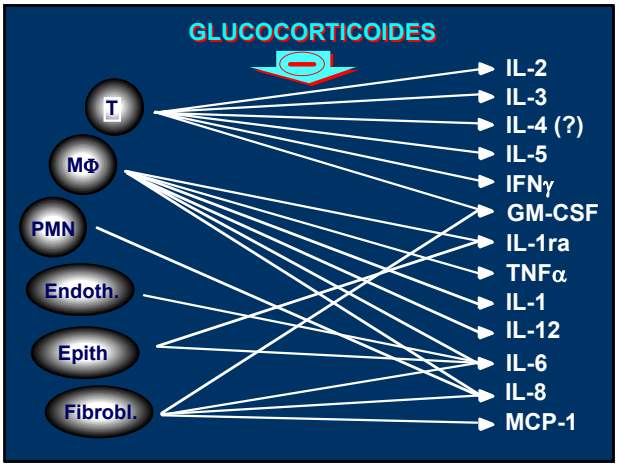
Tzung et al. Eur. J. Immunol. 1992, 22, 3097



GLUCOCORTICOIDS



GLUCOCORTICOIDES



GLUCOCORTICOIDES

monocyte / macrophage	CD14 — MHC classe II, TNF R (p75)
	Facteur Tissulaire (dépend de la nature de l'inducteur)
cellule endothéliale	ELAM-1, ICAM-1
T	LFA-1, CD2 (LFA-3) — IL-2 R, IL-6 R
cellule épithéliale	IL-6 R, TNF R (p55)
PMN	IL-1 R

GLUCOCORTICOIDS AND IL-10 EXPRESSION

Carbon tetrachloride induced hepatotoxicity — *Swain et al. 1999, J. Physiol. 276, G199*

Plasma IL-10 / Hepatic IL-10 mRNA; +RU486 (T-12 h & T0); 12 h

Cardiopulmonary bypass — *Tabardel et al. 1996, Surgery 119, 76*

T-4h: none, Dexamethasone, Methylprednisolone; IL-10 90 min; 0 100 200 300 400 500 pg/ml

Endotoxinemia — *Marchant et al. 1996, Clin Exp Imm 106, 91*

Serum IL-10 90 min post LPS 100 µg i.p. (ng/ml); methylprednisolone mg/kg (T-30 min)

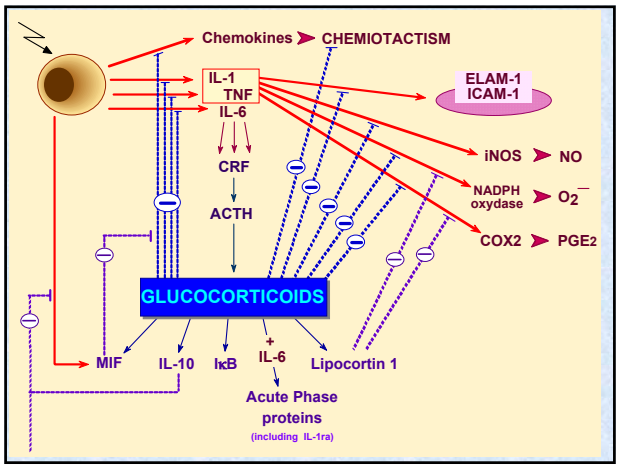
Methylpred. (1µg/ml) increases *in vitro* IL-10 production by per. MØ (+70%)

In vitro LPS activation — *Visser et al. 1998, Blood 91, 4255*; *Fushimi et al. 1997, Intern Arch All Immunol 112, 13*

Whole blood

PBMC: IL-10 mRNA expression : - 42 %; IL-10 production : - 61 %

IL-10 prod. is relatively insensitive. There is inter-individual heterogeneity



MIF AS A GLUCOCORTICOID-INDUCED MODULATOR OF CYTOKINE PRODUCTION

Calandra et al. Nature 1995, 377, 68

Rat → Dexamethasone (1 mg/kg) → GLUCOCORTICOIDS

MIF in plasma (peak 3 - 6 h)

hydrocortisone, Dexamethasoe 10^{-10} - 10^{-14} M

RAW 264-7 MØ → MIF in supernatant

MIF overrides glucocortico- mediated inhibition of cytol induction by LPS stimulated

T0 : human Mo + Dexamethasone ± MIF (1 ng/ml)
T+1h : LPS (1µg/ml)

% Inhibition: 0, 50, 100

MIF: 0; TNF: +; IL-8: +; IL-1: +; IL-6: +

EFFECT OF ANTI-MIF ON LPS INDUCED PULMONARY PMN ACCUMULATION

Makita et al. Am J Respi Crit Care Med 1998, 158, 573