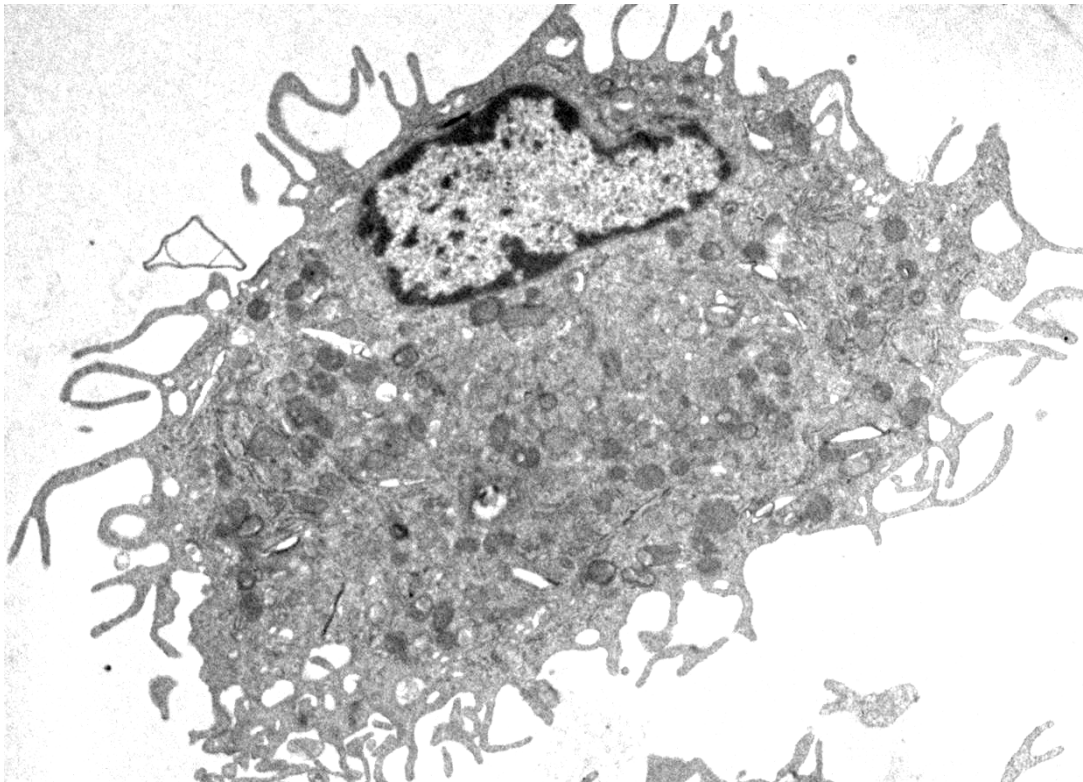


# Early steps regulating proliferation and activation in macrophages



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**Als meus pares, Àngel i Teresa, pel seu amor incondicional.**

**Al meu germà, Miquel-Àngel, per estar al meu costat.**

**I al lector, que la gaudeixi.**



Y qué más se puede pedir?

Quizá querer y nunca sufrir.

*Fangoria*. La diferencia entre la fe y la ciencia.

Arquitectura efímera.

A las masas que les parta un rayo,

nos dirigimos al hombre,

que es lo único que nos interesa.

*Antonio Machado (1875-1939)*

No es sabio el que sabe dónde está el tesoro,

Si no el que lo trabaja y lo saca.

*Francisco de Quevedo y Villegas (1580-1645)*

Nada se aprende a menos

Que aquello que ha de ser aprendido

Nos emocione y nos motive.

*Francisco Mora Teruel*





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## **ABBREVIATIONS**

- AP-1, activating protein-1  
Apaf-1, apoptosis protease-activating factor 1  
APC, antigen-presenting cell  
ATF2, activating transcription factor 2  
ARE, adenosine/uridine rich element  
ASK, apoptosis signal-regulating kinase  
ATF2, activating transcription factor 2  
BMDM, bone marrow derived macrophages  
BrdU, bromo-deoxy uridine  
Card, caspase recruitment domains  
CIITA, class II transactivator  
Cdk, cyclin-dependent kinase  
CDKI, Cdk inhibitor  
Cic, cyclin  
Cit c, cytochrome c  
C-Myc, cellular homologue of avian myeloblastosis virus oncogene  
CRE, cAMP-response element  
CREB, cAMP-response element binding protein  
CsA, cyclosporine A  
Cyp, cyclophilins  
DAG, 1, 2-diacylglycerol  
DD, death domain  
DMEM, Dulbecco's modified Eagle's medium  
dNTP, deoxyribonucleotide pool  
DSP, dual specificity phosphatase  
Elk-1, ETS-domain protein  
ER endoplasmic reticulum  
ERK, extracellular signal regulated kinase  
FCS, foetal calf serum  
FKBP, FK506 binding protein  
Foxo, forkhead transcription factor  
GAS, gamma-interferon activated sequence  
GEMM-CFU, granulocyte/erythrocyte/megakaryocyte/macrophage colony-forming unit  
GM-CFU, granulocyte-macrophage colony-forming unit  
GM-CSF, granulocyte-macrophage colony stimulating factor

## *Abbreviations*

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GTP, guanine triphosphate  
Hsp, heat shock protein  
HDAC, histone deacetylase  
IAP, inhibitor of apoptosis  
IFN- $\alpha/\beta$ , interferon alpha/beta  
IFN- $\gamma$ , interferon gamma  
IFN- $\gamma$ R, interferon gamma receptor  
IgG, immunoglobulin G  
I $\kappa$ B, NF- $\kappa$ B inhibitor  
IL, interleukin  
IL-XR, IL-X receptor  
IL-XRa, IL-X receptor antagonist  
IRAK, IL-1R-associated kinase  
IRF-1, immediate-early inducible factor  
JAK, Janus kinase  
JNK, c-jun NH2-terminal kinase  
KO, knock-out  
LBP, LPS binding protein  
LPS, lipopolysaccharide  
MAPK, mitogen-activated protein kinase  
MAPKAPK2, MAPK-activated protein kinase 2  
MAPKK, MAPK kinase  
MAPKKK, MAPKK kinase  
M-CSF, macrophage colony stimulating factor  
M-CSFR, M-CSF receptor  
MD-2, myeloid differentiation protein-2  
Mdm2, murine double minute 2, a p53-associated oncogene  
MEK, mitogen extracellular signal-related kinase  
MHC, major histocompatibility complex  
MKP, mitogen-activated protein kinase phosphatase  
NF-AT, nuclear factor activator of T lymphocytes  
NF- $\kappa$ B, nuclear factor immunoglobulin kappa chain enhancer B cell transcription  
NO, nitric oxide  
NOS2, inducible nitric oxide synthase  
p53, tumor suppressor protein  
PC, phosphatidylcholine  
PCNA, proliferating cell nuclear antigen

PDGF, platelet derived growth factor  
PDK, phosphoinositide-dependent kinase  
PI, phosphatidylinositol  
PI3K, phosphoinositide 3-kinase  
PI (4) P, phosphatidylinositol 4 monophosphate  
PI (4, 5) P<sub>2</sub>, phosphatidylinositol-4, 5-bisphosphate  
PIP<sub>3</sub>, (phosphatidylinositol (3, 4, 5)-triphosphate  
PKA, protein kinase A  
PKB, protein kinase B  
PKC, protein kinase C  
PLC-C<sub>γ</sub>, phospholipase C-gamma  
PPIase, peptidyl prolyl cis-trans isomerase  
pRb, retinoblastoma tumor suppressor gene  
PSP, Serine/threonine-specific phosphatase  
PTEN, phosphatase and tensin homologue  
PTP, tyrosine-specific phosphatase  
Rapa, Rapamycin  
SAPK, stress activated protein kinase  
SfA, Sanglifehrin A  
SEK, SAPK/ERK kinase  
SH2, src-homology 2 domain  
STAT, signal transducer and activator of transcription  
TAP, transporter associated with antigen processing  
TGF- $\beta$ , transforming growth factor- $\beta$   
TCR, lymphocyte T cell receptor  
Th, T helper  
TIR domain, Toll/IL-1 receptor/plant R gene product homology domain  
TIRAP/Mal, Toll receptor IL-1R domain with adaptor protein/aka MyD88-adaptor like  
TLR, Toll-like receptor  
TNF, tumor necrosis factor  
Tpl-2, tumor progresión locus 2  
Tollip, Toll-interacting protein  
TPA, 2-O-tetradecanoyl-phorbol-13-acetate, phorbol ester  
WAF, wild-type p53-activated factor



## APPENDIX

### Inhibitors used

PRODUCT	PROPERTIES	OBTAINED IN
5-aza-2'-deoxycytosine (AC)	Methylases inhibitor	Tocris, Bristol, UK
Actinomycin D	RNA synthesis inhibitor	Sigma, St. Louis, MO
Cyclosporine A (CsA)	Calcineurin Inhibitor	Novartis, Basel, Switzerland
FK506 (Tacrolimus)	Calcineurin Inhibitor	Novartis, Basel, Switzerland
Geldanamycin	Raf inhibitor	Calbiochem, San Diego, CA
GF109203X (GF)	Conventional and novel PKC inhibitor	Calbiochem, San Diego, CA
Gö6976 (Gö)	PKC $\alpha$ and $\beta$ 1 inhibitor	Calbiochem, San Diego, CA
KT 5720	PKA inhibitor	Calbiochem, San Diego, CA
Lactacystin (Lacta)	Proteasome inhibitor	Calbiochem, San Diego, CA
LY294002 (LY)	PI3K inhibitor	Sigma Chemical, St. Louis, MO
Nocodazole (Noco)	G2/M Microtubule interference anticancer drug	Sigma Chemical, St. Louis, MO
PD98059 (PD)	MEK-1/2 inhibitor	New England Biolabs. Beberly, MA
PSI	Proteasome inhibitor	Calbiochem, San Diego, CA
Rapamycin (Rapa)	p70S6K and mTOR inhibitor	Novartis, Basel, Switzerland
Sodium arsenite (SA)	Raf-1 inhibitor	Wako Pure Chemicals, Osaka, Japon
SB203580 (SB)	p38MAPK inhibitor	Calbiochem, San Diego, CA
SP600125 (SP)	JNK1, 2, 3 inhibitor	Tocris, Bristol, UK
Trichostatin (TSA)	Deacetylases inhibitor	Tocris, Bristol, UK
Wortmannin (Wort)	PI3K inhibitor	Sigma Chemical, St. Louis, MO
ZM336372 (ZM)	c-Raf inhibitor	Calbiochem, San Diego, CA