

Teil VI

Anhang

14 Abkürzungsverzeichnis

AEL	Antitumor-Etherlipide
AG	Arbeitsgruppe
AP1/2	activator protein 1/2
APC	Alkylphosphocholin
ATL	Antitumor-Lipid
ATP	Adenosintriphosphat
BCA	Bicinchonin-4-carbonsäure
BrdU	5-Brom-2'-desoxyuridin
BSA	bovines Serumalbumin
cAMP	cyclisches Adenosinmonophosphat
CDP	Cytidindiphosphat
C/EBP	CCAAT/enhancer binding protein
CMC	critical micelle concentration
CMP	Cytidinmonophosphat
CoA	Coenzym A
CPITC	Coumarin-phalloidin Isothiocyanat
CTP	Cytidintriphosphat
Cy2	Carbocyanin 2
DAG	Diacylglycerol
DGK	Diacylglycerol-Kinase
DMSO	Dimethylsulfoxid
DNA	Desoxyribonukleinsäure
DPH	Diphenylhexatrien
DTT	Dithiothreitol
EC ₅₀	effective concentration die Konzentration, bei der die Hälfte der Zellen, tot ist
EGF	epidermal growth factor
EDTA	Ethyldiamintetraacetat
EGTA	Ethylenglycol-bis(2-aminoethyl)tetraessigsäure
ELISA	enzyme linked immunosorbent assay
ERK	extracellular signal-regulated kinase
ET-18-OCH ₃	razemisches 1-octadecyl-2-methyl- <i>sn</i> -glycero-3-phosphocholin
EZM	extrazelluläre Matrix
FACS	fluorescence-activated cell scanning
FAK	focal adhesion kinase

FCS	fetal calf serum
FITC	Fluoresceinisothiocyanat
GAP	GTPase activating protein
GDP	Guanosindiphosphat
GEF	guanosin nucleotide exchange factor
GF/C-Filter	glass fibre/cotton-Filter
GFP	grün-fluoreszierendes Protein
Glc	glucose
GM-CSF	Granulozyten-Makrophagen - Kolonie-stimulierender Faktor
GPC	Glycerylphosphorylcholin
GTP	Guanosintriphosphat
HaCaT	human adult keratinocytes kept in high calcium at low temperature
HEMA	Hydroxyethyl-methyl-acrylat
HePC	Hexadecylphosphocholin
Hepes	N-[2-Hydroxyethyl]piperazin-N'-[2-ethansulfonsäure]
HePS	Hexadecylphosphoserin
HLA	human leukocyte antigen protein
HLB	hydrophilic-lipophilic balance
IB	Immunoblot
IC ₅₀	inhibitory concentration
Ig	die Konzentration, bei der das Zellwachstum um die Hälfte reduziert ist
IL	Immunglobulin
Ino-C2-PAF	Interleukin
IP3	Inositol-C2-PAF
kDa	Inositoltrisphosphat
LDH	Kilodalton
LPA	Lactat-Dehydrogenase
mAb	lyso phosphatidic acid
MALDI-TOF-MS	monoclonal antibody
MAPK	matrix-assisted laser-desorption-ionisation time-of-flight
MEK	mass spectrometry
MHC	Mitogen-aktivierte Proteinkinase
MOTC	MAP/ERK-Kinase
MM46	major histocompatibility complex
mRNA	microtubule organising center
MTP	Myelom der Maus
MW	messenger RNA
NADP	Mikrotiterplatte
NE	molecular weight
NK-Zellen	Nikotinamid-Adenin-Dinukleotid
OD	Nanoemulsion
	natural killer-Zellen
	optische Dichte

PA	phosphatidic acid
pAb	polyclonal antibody
PAF	Plättchen-aktivierender Faktor
PAF-R	Plättchen-aktivierender Faktor - Rezeptor
pbmc	peripheral mononuclear blood cells
PBS	phosphate-buffered saline
PC	Phosphatidylcholin
PC5	PE-Cyanin 5
PCS	photon correlation spectroscopy
PE	Phycoerythrin
PerCP	peridinin chlorophyll protein cyanin 5.5
PHA	Phytohämagglutinin
PI	Propidiumiodid
PI	Polydispersitätsindex
PIDS	polarisation intensity differential scattering
PI3-K	Phosphoinositid-3-Kinase
PIP2	Phosphatidyl-inositol-4,5-bisphosphat
PC-PLC	Phosphocholin-spezifische PLC
PI-PLC	Phosphoinositid-spezifische PLC
PKA	Proteinkinase A
PKB	Proteinkinase B
PKC	Proteinkinase C
PLC	Phospholipase C
PLD	Phospholipase D
PMA	Phorbol-12-myristyl-13-acetat
PMSF	Phenylmethylsulfonylfluorid
POD	Peroxidase
PUVA	Psoralen und UV-A Strahlung
RNA	ribonuleic acid
ROCK	Rho-assoziierte Kinasen
rpm	rounds per minute
RT	Raumtemperatur
S180	Sarkom der Maus
SCC	squamous cell carcinoma
SDS	sodium dodecyl sulfate
SDS-PAGE	SDS-Polyacrylamid-Gelelektrophorese
Sp1	trans-activating transcription factor 1
SPL	synthetische Phospholipide
STAT	signal transducer and activator of transcription
TCA	Trichloressigsäure
TBS	Tris-buffered saline
TEMED	N;N;N';N'-Tetramethylenediamin
TNF α	Tumornekrosefaktor α

Tris	Tris(hydroxymethyl)aminomethan
TRITC	Tetramethylenrhodamin-Isothiocyanat
UKBF	Universitätsklinikum Benjamin Franklin
UV	Ultraviolett
X5563	Myelom der Maus
ZNS	zentrales Nervensystem

15 Literaturverzeichnis

- Adams, J. C. and F. M. Watt (1988). 'An unusual strain of human keratinocytes which do not stratify or undergo terminal differentiation in culture.' J Cell Biol **107**(5): 1927-38.
- Akiba, S. and T. Sato (2004). 'Cellular Function of Calcium-Independent Phospholipase A2.' Biol. Phar. Bull. **27**(8):1174-1178
- Alappatt, C., C. A. Johnson, et al. (2000). 'Acute keratinocyte damage stimulates platelet- activating factor production.' Arch Dermatol Res **292**(5): 256-9.
- Alonso, L. and E. Fuchs (2003). 'Stem cells of the skin epithelium.' Proc Natl Acad Sci USA **100 Suppl 1:** 11830-5.
- Andreesen, R., M. Modolell, et al. (1978). 'Selective destruction of human leukemic cells by alkyl-lysophospholipids.' Cancer Res **38**(11 Pt 1): 3894-9.
- Andreesen, R., M. Modolell, et al. (1979). 'Selective sensitivity of chronic myelogenous leukemia cell populations to alkyl-lysophospholipids.' Blood **54**(2): 519-23.
- Andreesen, R., M. Modolell, et al. (1983). 'Temperature dependence of leukemic cell destruction by alkyl-lysophospholipids (NSC 324368).' Exp Hematol **11**(6): 564-70.
- Andreesen, R., J. Osterholz, et al. (1984). 'Tumor cytotoxicity of human macrophages after incubation with synthetic analogues of 2-lysophosphatidylcholine.' J Natl Cancer Inst **72**(1): 53-9.
- Andreesen, R. and V. Giese (1987). 'Differential effects of ether lipids on the activity and secretion of interleukin-1 and interleukin-2.' Lipids **22**(11): 836-41.
- Arnold, B., F. G. Staber, et al. (1979). 'Lysolecithin analogs as adjuvants in delayed-type hypersensitivity in mice. II. Studies on the mode of action.' Eur J Immunol **9**(5): 367- 70.
- Arthur, G. and R. Bittman (1998). 'The inhibition of cell signaling pathways by antitumor ether lipids.' Biochim Biophys Acta **1390**(1): 85-102.
- Attard, G. S., R. H. Templer, et al. (2000). 'Modulation of CTP:phosphocholine cytidylyltransferase by membrane curvature elastic stress.' Proc Natl Acad Sci USA **97**(16): 9032-6.

- Baden, H. P., J. K. Kubilus, et al. (1987). 'Characterization of monoclonal antibodies generated to the cornified envelope of human cultured keratinocytes.' J Invest Dermatol **89**(5): 454-9.
- Bador, H., R. Morelis, et al. (1983). 'Biochemical evidence for the role of alkyl-lysophospholipids on liver sialyltransferase.' Int J Biochem **15**(9): 1137-42.
- Bazill, G. W. and T. M. Dexter (1990). 'Role of endocytosis in the action of ether lipids on WEHI-3B, HL60, and FDCP-mix A4 cells.' Cancer Res **50**(23): 7505-12.
- Bazzoni, G. and M. E. Hemler (1998). 'Are changes in integrin affinity and conformation overemphasized?' Trends Biochem Sci **23**(1): 30-4.
- Benveniste, J., M. Tence, et al. (1979). '[Semi-synthesis and proposed structure of platelet- activating factor (P.A.F.): PAF-acether an alkyl ether analog of lysophosphatidylcholine].' C R Seances Acad Sci D **289**(14): 1037-40.
- Berdel, W. E., W. R. Bausert, et al. (1980). 'The influence of alkyl-lysophospholipids and lysophospholipid-activated macrophages on the development of metastasis of 3-Lewis lung carcinoma.' Eur J Cancer **16**(9): 1199-204.
- Berdel, W. E., W. R. Bausert, et al. (1981). 'Anti-tumor action of alkyl-lysophospholipids (Review).' Anticancer Res **1**(6): 345-52.
- Berdel, W. E., H. Schlehe, et al. (1982). 'Early tumor and leukemia response to alkyllysophospholipids in a phase I study.' Cancer **50**(10): 2011-5.
- Berdel, W. E., M. Fromm, et al. (1983). 'Cytotoxicity of thioether-lysophospholipids in leukemias and tumors of human origin.' Cancer Res **43**(11): 5538-43.
- Berdel, W. E., E. Greiner, et al. (1984). 'Cytotoxic effects of alkyl-lysophospholipids in human brain tumor cells.' Oncology **41**(2): 140-5.
- Berdel, W. E., U. Fink, et al. (1987). 'Clinical phase I pilot study of the alkyl lysophospholipid derivative ET-18-OCH₃.' Lipids **22**(11): 967-9.
- Berggren, M. I., A. Gallegos, et al. (1993). 'Inhibition of the signalling enzyme phosphatidylinositol-3-kinase by antitumor ether lipid analogues.' Cancer Res **53**(18): 4297-302.
- Bergmann, J., I. Junghahn, et al. (1994). 'Multiple effects of antitumor alkyl-lysophospholipid analogs on the cytosolic free Ca²⁺ concentration in a normal and a breast cancer cell line.' Anticancer Res **14**(4A):1549-56.
- Berkovic, D., E. A. Fleer, et al. (1992). 'Effects of hexadecylphosphocholine on cellular function.' Prog Exp Tumor Res **34**: 59-68.

Bittman, R., H. S. Byun, et al. (1997). 'Enantioselective synthesis and antiproliferative properties of an ilmofosine analog, 2'-(trimethylammonio)ethyl 3-(hexadecyloxy)-2- (methoxymethyl)propyl phosphate, on epithelial cancer cell growth.' *J Med Chem* **40**(9): 1391-5.

Bleck, O., D. Abeck, et al. (1999). 'Two ceramide subfractions detectable in Cer(AS) position by HPTLC in skin surface lipids of non-lesional skin of atopic eczema.' *J Invest Dermatol* **113**(6): 894-900.

Boelsma, E., M. C. Verhoeven, et al. (1999). 'Reconstruction of a human skin equivalent using a spontaneously transformed keratinocyte cell line (HaCaT).' *J Invest Dermatol* **112**(4): 489-98.

Bonina F. P., L. Montenegro, N. Scrofani, E. Esposito, R. Cortesi, E. Menegatti and C. Nastruzzi (1995) 'Effects of phospholipid based formulations on in vitro and in vivo percutaneous absorption of methyl nicotinate' *J. Control. Release* **34**:53-63

Botzler, C., H. J. Kolb, et al. (1996). 'Noncytotoxic alkyl-lysophospholipid treatment increases sensitivity of leukemic K562 cells to lysis by natural killer (NK) cells.' *Int J Cancer* **65**(5):633-8.

Boukamp, P., R. T. Petrussevska, et al. (1988). 'Normal keratinization in a spontaneously immortalized aneuploid human keratinocyte cell line.' *J Cell Biol* **106**(3): 761-71.

Bouwstra, J. A., P. L. Honeywell-Nguyen, et al. (2003). 'Structure of the skin barrier and its modulation by vesicular formulations.' *Prog Lipid Res* **42**(1): 1-36.

Brachwitz, H. and C. Vollgraf (1995). 'Analogs of alkyllysophospholipids: chemistry, effects on the molecular level and their consequences for normal and malignant cells.' *Pharmacol Ther* **66**(1): 39-82.

Bratton, D. L., E. Dreyer, et al. (1992). 'The mechanism of internalization of platelet-activating factor in activated human neutrophils. Enhanced transbilayer movement across the plasma membrane.' *J Immunol.* **151**:148(2):514-23.

Budd, R. C. (2002). 'Death receptors couple to both cell proliferation and apoptosis.' *J Clin Invest* **109**(4): 437-41.

Bunch, J., M. R. Clench, et al. (2004). 'Determination of pharmaceutical compounds in skin by imaging matrix-assisted laser desorption/ionisation mass spectrometry.' *Rapid Commun Mass Spectrom* **18**(24): 3051-60.

Buxman, M. M. and K. D. Wuepper (1975). 'Keratin cross-linking and epidermal transglutaminase. A review with observations on the histochemical and immunohistochemical localization of the enzyme.' *J Invest Dermatol* **65**(1): 107-12.

- Capek, I. (2004). 'Degradation of kinetically-stable o/w emulsions.' Adv Colloid Interface Sci **107**(2-3): 125-55.
- Carman, C. V. and T. A. Springer (2003). 'Integrin avidity regulation: are changes in affinity and conformation underemphasized?' Curr Opin Cell Biol **15**(5): 547-56.
- Caron, E. (2003). 'Rac signalling: a radical view.' Nat Cell Biol **5**(3): 185-7.
- Carpenter, C. B. (1982). 'Autoimmunity and HLA.' J Clin Immunol **2**(3): 157-65.
- Carreño, B. M. and M. Collins (2002). 'The B7 family of ligands and its receptors: new pathways for costimulation and inhibition of immune responses.' Annu Rev Immunol **20**: 29-53.
- Carrigues, B., G. Bertrand (1984). Synthesis **870**
- Carroll, J. M., M. R. Romero, et al. (1995). 'Suprabasal integrin expression in the epidermis of transgenic mice results in developmental defects and a phenotype resembling psoriasis.' Cell **83**(6): 957-68.
- Cau, J. and A. Hall (2005). 'Cdc42 controls the polarity of the actin and microtubule cytoskeletons through two distinct signal transduction pathways.' J Cell Sci **118**(Pt 12): 2579-87.
- Chaturvedi, V., J. Z. Qin, et al. (1999). 'Apoptosis in proliferating, senescent, and immortalized keratinocytes.' J Biol Chem **274**(33): 23358-67.
- Chinnaiyan, A. M., K. O'Rourke, et al., (1995). 'FADD, a novel death domain-containing protein, interacts with the death domain of Fas and initiates apoptosis.' Cell **81**(4):505-12.
- Clevers, H., S. Dunlap, et al. (1988). 'The transmembrane orientation of the epsilon chain of the TcR/CD3 complex.' Eur J Immunol **18**(5): 705-10.
- Clive, S., J. Gardiner, et al. (1999). 'Miltefosine as a topical treatment for cutaneous metastases in breast carcinoma.' Cancer Chemother Pharmacol **44** Suppl: S29-30.
- Cocco, L., L. Manzoli, et al. (2004). 'Significance of subnuclear localization of key players of inositol lipid cycle.' Adv Enzyme Regul **44**: 51-60.
- Danhauser-Riedl, S., A. Himmelmann, et al. (1990). 'Cytotoxic effects of hexadecylphosphocholine in neoplastic cell lines including drug-resistant sublines in vitro.' J Lipid Mediat **2**(5): 271-80.
- Darzynkiewicz, Z., G. Juan, et al. (1997). 'Cytometry in cell necrobiology: analysis of apoptosis and accidental cell death (necrosis).' Cytometry **27**(1): 1-20.

- DeMali, K. A., C. A. Barlow, et al. (2002). 'Recruitment of the Arp2/3 complex to vinculin: coupling membrane protrusion to matrix adhesion.' *J Cell Biol* **159**(5): 881-91.
- Demopoulos, C. A., R. N. Pinckard, et al. (1979). 'Platelet-activating factor. Evidence for 1- O-alkyl-2-acetyl-sn-glyceryl-3-phosphorylcholine as the active component (a new class of lipid chemical mediators).' *J Biol Chem* **254**(19): 9355-8.
- Detmar, M., C. C. Geilen, et al. (1994). 'Phospholipid analogue hexadecylphosphocholine inhibits proliferation and phosphatidylcholine biosynthesis of human epidermal keratinocytes in vitro.' *J Invest Dermatol* **102**(4): 490-4.
- Diezel, W., B. Volc-Platzer, et al. (1985). '[Regulation of the immune response—findings on the significance of HLA-DR antigens]' *Dermatol Monatsschr* **171**(5): 303-7.
- Diomede, L., F. Colotta, et al. (1993). 'Induction of apoptosis in human leukemic cells by the ether lipid 1-octadecyl-2-methyl-rac-glycero-3-phosphocholine. A possible basis for its selective action.' *Int J Cancer* **53**(1): 124-30.
- Diomede, L., B. Piovani, et al. (1993) 'The effect of culture medium composition on ether lipid cytotoxic activity.' *Lipids* **28**(3):189-92.
- Dotto, G. P. (1999). 'Signal transduction pathways controlling the switch between keratinocyte growth and differentiation.' *Crit Rev Oral Biol Med* **10**(4): 442-57.
- Dowling, J., Q. C. Yu, et al. (1996). 'Beta4 integrin is required for hemidesmosome formation, cell adhesion and cell survival.' *J Cell Biol* **134**(2): 559-72.
- Dy, L. C., Y. Pei, et al. (1999). 'Augmentation of ultraviolet B radiation-induced tumor necrosis factor production by the epidermal platelet-activating factor receptor.' *J Biol Chem* **274**(38): 26917-21.
- Eckert, R. L. and J. F. Welter (1996). 'Transcription factor regulation of epidermal keratinocyte gene expression.' *Mol Biol Rep* **23**(1): 59-70.
- Eckert, R. L., J. F. Crish, et al. (2004). 'Regulation of involucrin gene expression.' *J Invest Dermatol* **123**(1): 13-22.
- Egberts, F., M. Heinrich, et al. (2004). 'Cathepsin D is involved in the regulation of transglutaminase 1 and epidermal differentiation.' *J Cell Sci* **117**(Pt 11): 2295-307.
- Ekblom, M., M. Falk, et al. (1998). 'Laminin isoforms and epithelial development.' *Ann NY Acad Sci* **857**: 194-211.
- Entschladen, F., T. L. t. Drell, et al. (2005). 'Analysis methods of human cell migration.' *Exp Cell Res* **307**(2): 418-26.

- Epand, R. M. and D. S. Lester (1990). 'The role of membrane biophysical properties in the regulation of protein kinase C activity.' Trends Pharmacol Sci **11**(8): 317-20.
- Esmann, J., J. J. Voorhees, et al. (1989). 'Increased membrane-associated transglutaminase activity in psoriasis.' Biochem Biophys Res Commun **164**(1): 219-24.
- Fisher, S. K., A. M. Heacock, et al. (1992). 'Inositol lipids and signal transduction in the nervous system: an update.' J Neurochem **58**(1): 18-38.
- Fleer, E. A., D. J. Kim, et al. (1990). 'Cytotoxic activity of lysophosphatidylcholine analogues on human lymphoma Raji cells.' Onkologie **13**(4): 295-300.
- Fleer, E. A., D. Berkovic, et al. (1992). 'Cellular uptake and metabolic fate of hexadecylphosphocholine.' Prog Exp Tumor Res **34**: 33-46.
- Fleer, E. A., D. Berkovic, et al. (1993). 'Investigations on the cellular uptake of hexadecylphosphocholine.' Lipids **28**(8): 731-6.
- Fuchs, E. (1990). 'Epidermal differentiation: the bare essentials.' J Cell Biol **111**(6 Pt 2): 2807-14.
- Fuchs, E. and C. Byrne (1994). 'The epidermis: rising to the surface.' Curr Opin Genet Dev **4**(5): 725-36.
- Fujiwaki, T., S. Yamaguchi, et al. (2002). 'Application of delayed extraction matrix-assisted laser desorption ionization time-of-flight mass spectrometry for analysis of sphingolipids in cultured skin fibroblasts from sphingolipidosis patients.' Brain Dev **24**(3): 170-3.
- Gabriel, B. (1999). 'Integrin-vermittelte Signaltransduktionsmechanismen in HaCaT-Zellen.' Dissertation FB Humanmedizin, FU Berlin
- Gajate, C., A. M. Santos-Beneit, et al. (2000). 'Involvement of mitochondria and caspase-3 in ET-18-OCH(3)-induced apoptosis of human leukemic cells.' Int J Cancer **86**(2): 208-18.
- Gajate C., E. Del Canto-Janez, et al. (2004). 'Intracellular triggering of Fas aggregation and recruitment of apoptotic molecules into Fas-enriched rafts in selective tumor cell apoptosis.' J Exp Med **200**(3):353-65.
- Gan, X. H. and B. Bonavida (1999). 'Preferential induction of TNF-alpha and IL-1beta and inhibition of IL-10 secretion by human peripheral blood monocytes by synthetic aza- alkyl lysophospholipids.' Cell Immunol **193**(2): 125-33.
- Gandarillas, A. and F. M. Watt (1995). 'Changes in expression of members of the fos and jun families and myc network during terminal differentiation of human keratinocytes.' Oncogene **11**(7): 1403-7.

- Geilen, C. C., R. Haase, et al. (1991). 'The phospholipid analogue, hexadecylphosphocholine, inhibits protein kinase C in vitro and antagonises phorbol ester-stimulated cell proliferation.' *Eur J Cancer* **27**(12): 1650-3.
- Ghafourifar, P., S. D. Klein, et al. (1999). 'Ceramide induces cytochrome c release from isolated mitochondria. Importance of mitochondrial redox state.' *J Biol Chem* **274**(10): 6080-4.
- Gloor, M. (2004). 'How do dermatological vehicles influence the horny layer?' *Skin Pharmacol Physiol* **17**(6): 267-73.
- Gniadecki, R. and M. J. Calverley (2002). 'Emerging drugs in psoriasis.' *Expert Opin Emerg Drugs* **7**(1): 69-90.
- Gong, J., F. Traganos, et al. (1994). 'A selective procedure for DNA extraction from apoptotic cells applicable for gel electrophoresis and flow cytometry.' *Anal Biochem* **218**(2): 314-9.
- Gottlieb, A. B. (1988). 'Immunologic mechanisms in psoriasis.' *J Am Acad Dermatol* **18**(6): 1376-80.
- Grosman, N. (1990). 'Ether lipid (AMG) exhibits both synergistic and inhibitory interactions with the ionophore A23187 in mast cell histamine release.' *Immunopharmacology* **19**(2): 113-9.
- Guivisdalsky, P. N., R. Bittman, et al. (1990). 'Synthesis and antineoplastic properties of ether-linked thioglycolipids.' *J Med Chem* **33**(9): 2614-21.
- Gutjahr, M. C., J. Rossy, et al. (2005). 'Role of Rho, Rac, and Rho-kinase in phosphorylation of myosin light chain, development of polarity, and spontaneous migration of Walker 256 carcinosarcoma cells.' *Exp Cell Res* **308**(2): 422-38.
- Hanahan, D. J. (1986). 'Platelet activating factor: a biologically active phosphoglyceride.' *Annu Rev Biochem* **55**: 483-509.
- Heesbeen, E. C., L. F. Verdonck, et al. (1991). 'Alkyllysophospholipid ET-18-OCH₃ acts as an activator of protein kinase C in HL-60 cells.' *FEBS Lett* **290**(1-2): 231-4.
- Helpman, D. M., K. C. Barnes, et al. (1983). 'Phospholipid-sensitive Ca²⁺-dependent protein phosphorylation system in various types of leukemic cells from human patients and in human leukemic cell lines HL60 and K562, and its inhibition by alkyllysophospholipid.' *Cancer Res* **43**(6): 2955-61.
- Herrmann, D. B. and H. A. Neumann (1986). 'Cytotoxic ether phospholipids. Different affinities to lysophosphocholine acyltransferases in sensitive and resistant cells.' *J Biol Chem* **261**(17): 7742-7.

- Hilgard, P., J. Stekar, et al. (1988). 'Characterization of the antitumor activity of hexadecylphosphocholine (D 18506).' Eur J Cancer Clin Oncol **24**(9): 1457-61.
- Hilgard, P. (1990). 'New pharmaceuticals: miltefosine.' Anticancer Drugs **1**(2): 185.
- Hilgard, P., E. Kampherm, et al. (1991). 'Investigation into the immunological effects of miltefosine, a new anticancer agent under development.' J Cancer Res Clin Oncol **117**(5): 403-8.
- Hilgard, P., J. Stekar, et al. (1992). 'Experimental therapeutic studies with miltefosine in rats and mice.' Prog Exp Tumor Res **34**: 116-30.
- Hill, C. S. and R. Treisman (1995). 'Transcriptional regulation by extracellular signals: mechanisms and specificity.' Cell **80**(2): 199-211.
- Hill, C. S., J. Wynne, et al. (1995). 'The Rho family GTPases RhoA, Rac1, and CDC42Hs regulate transcriptional activation by SRF.' Cell **81**(7): 1159-70.
- Himmelmann, A. W., S. Danhauser-Riedl, et al. (1990). 'Cross-resistance pattern of cell lines selected for resistance towards different cytotoxic drugs to membrane-toxic phospholipids in vitro.' Cancer Chemother Pharmacol **26**(6): 437-43.
- Hintermann, E., M. Bilban, et al. (2001). 'Inhibitory role of alpha 6 beta 4-associated erbB-2 and phosphoinositide 3-kinase in keratinocyte haptotactic migration dependent on alpha 3 beta 1 integrin.' J Cell Biol **153**(3):465-78.
- Hoffman, D. R., J. Hajdu, et al. (1984). 'Cytotoxicity of platelet activating factor and related alkyl-phospholipid analogs in human leukemia cells, polymorphonuclear neutrophils, and skin fibroblasts.' Blood **63**(3): 545-52.
- Honda, Z., S. Ishii, et al. (2002). 'Platelet-activating factor receptor.' J Biochem (Tokyo) **131**(6): 773-9.
- Honma, Y., T. Kasukabe, et al. (1981). 'Induction of differentiation of cultured human and mouse myeloid leukemia cells by alkyl-lysophospholipids.' Cancer Res **41**(8): 3211-6.
- Hotchin, N. A., A. Gandarillas, et al. (1995). 'Regulation of cell surface beta 1 integrin levels during keratinocyte terminal differentiation.' J Cell Biol **128**(6): 1209-19.
- Houlihan, W. J., M. Lohmeyer, et al. (1995). 'Phospholipid antitumor agents.' Med Res Rev **15**(3): 157-223.
- Houlihan, W. J., K. Prasad, et al. (1996). 'Antitumor activity of the R- and S-enantiomers of RS-2-[[hydroxy[[2-[(octadecyloxy)methyl]tetrahydrofuran-2-yl]methoxy]-phosphinyl]oxy]-N, N,N,-trimethylethylaminium hydroxide inner salt.' J Med Chem **39**(2): 605-8.

- Humphries, M. J. (1996). 'Integrin activation: the link between ligand binding and signal transduction.' Curr Opin Cell Biol **8**(5): 632-40.
- Hynes, R. O. (2002). 'Integrins: bidirectional, allosteric signaling machines.' Cell **110**(6): 673-87.
- Igarashi, Y., K. Kitamura, et al. (1990). 'A role of lyso-phosphatidylcholine in GM3-dependent inhibition of epidermal growth factor receptor autophosphorylation in A431 plasma membranes.' Biochem Biophys Res Commun **172**(1): 77-84.
- Inoue, N., K. Hirata, et al. (1992). 'Lysophosphatidylcholine inhibits bradykinin-induced phosphoinositide hydrolysis and calcium transients in cultured bovine aortic endothelial cells.' Circ Res **71**(6): 1410-21.
- Ishaq, K. S., M. Capobianco, et al. (1989). 'Synthesis and biological evaluation of ether-linked derivatives of phosphatidylinositol.' Pharm Res **6**(3): 216-24.
- Ishii, S., T. Nagase, et al. (1997). 'Bronchial hyperreactivity, increased endotoxin lethality and melanocytic tumorigenesis in transgenic mice overexpressing platelet-activating factor receptor.' Embo J **16**(1): 133-42.
- Ishii, S. and T. Shimizu (2000). 'Platelet-activating factor (PAF) receptor and genetically engineered PAF receptor mutant mice.' Prog Lipid Res **39**(1): 41-82.
- Ishizaki, T., M. Uehata, et al. (2000). 'Pharmacological properties of Y-27632, a specific inhibitor of rho-associated kinases.' Mol Pharmacol **57**(5): 976-83.
- Izaki, S., T. Yamamoto, et al. (1996). 'Platelet-activating factor and arachidonic acid metabolites in psoriatic inflammation.' Br J Dermatol **134**(6): 1060-4.
- Izumi, T. and T. Shimizu (1995). 'Platelet-activating factor receptor: gene expression and signal transduction.' Biochim Biophys Acta **1259**(3): 317-33.
- Jha, T. K., S. Sundar, et al. (1999). 'Miltefosine, an oral agent, for the treatment of Indian visceral leishmaniasis.' N Engl J Med **341**(24): 1795-800.
- Jung, E. M., S. Betancourt-Calle, et al. (1999). 'Sustained phospholipase D activation is associated with keratinocyte differentiation.' Carcinogenesis **20**(4): 569-76.
- Kagedal, K., M. Zhao, et al. (2001). 'Sphingosine-induced apoptosis is dependent on lysosomal proteases.' Biochem J **359**(Pt 2): 335-43.
- Kalinin, A. E., A. V. Kajava et al. (2002). 'Epithelial barrier function: assembly and structural features of the cornified cell envelope.' BioEssay **24**:789-800.
- Kashiwagi, M., M. Ohba, et al. (2002). 'Protein kinase C eta (PKC eta): its involvement in keratinocyte differentiation.' J Biochcm (Tokyo) **132**(6): 853-7.

Kelley, E. E., E. J. Modest, et al. (1993). 'Unidirectional membrane uptake of the ether lipid antineoplastic agent edelfosine by L1210 cells.' Biochem Pharmacol **45**(12): 2435-9.

Korting, H. C., A. Unholzer, et al. (2002). 'Different skin thinning potential of equi-potent medium-strength glucocorticoids.' Skin Pharmacol Appl Skin Physiol **15**(2): 85-91.

Kosano, H., Y. Yasutomo, et al. (1990). 'Inhibition of estradiol uptake and transforming growth factor alpha secretion in human breast cancer cell line MCF-7 by an alkyl- lysophospholipid.' Cancer Res **50**(11): 3172-5.

Kreilgaard, M. (2002). 'Influence of microemulsions on cutaneous drug delivery.' Adv Drug Deliv Rev **54 Suppl 1**: S77-98.

Kriwet, K., C. C. Müller-Goymann (1995). 'Diclofenac release from phospholipid drug systems and permeation through excised human stratum corneum' Int. J. Pharm. **125** (2): 231-242

Kudo, I., S. Nojima, et al. (1987). 'Antitumor activity of synthetic alkylphospholipids with or without PAF activity.' Lipids **22**(11): 862-7.

Kung, A. L., A. Zetterberg, et al. (1990). 'Cytotoxic effects of cell cycle phase specific agents: result of cell cycle perturbation.' Cancer Res **50**(22): 7307-17.

Kwon, G. S. (2003). 'Polymeric micelles for delivery of poorly water-soluble compounds.' Crit Rev Ther Drug Carrier Syst **20**(5): 357-403.

Lam, A. C., R. S. Schlechter, (1987) 'The theory of diffusion in microemulsions.' J. Colloid Interface Sci. **120**: 56-63.

Leroy, A., G. K. de Bruyne, et al. (2003). 'Alkylphospholipids reversibly open epithelial tight junctions.' Anticancer Res **23**(1A): 27-32.

Liu, B. J., M. R. Zheng, et al. (1994). 'Effects of antipsoriatic drugs on biosynthesis of platelet activating factor by human keratinocytes.' Chin Med J (Engl) **107**(5): 326-31.

Lohmeyer, M. and P. Workman (1995). 'Growth arrest vs direct cytotoxicity and the importance of molecular structure for the in vitro anti-tumour activity of ether lipids.' Br J Cancer **72**(2): 277-86.

Lucas, L., R. Hernandez-Alcoceba, et al. (2001). 'Modulation of phospholipase D by hexadecylphosphorylcholine: a putative novel mechanism for its antitumoral activity.' Oncogene **20**(9): 1110-7.

- Maddala, R., V. N. Reddy, et al. (2003). 'Growth factor induced activation of Rho and Rac GTPases and actin cytoskeletal reorganization in human lens epithelial cells.' Mol Vis **9**: 329-36.
- Maekawa, M., T. Ishizaki, et al. (1999). 'Signaling from Rho to the actin cytoskeleton through protein kinases ROCK and LIM-kinase.' Science **285**(5429): 895-8.
- Mahdi, T., J. Tanzer, et al. (1995). 'Cell-mediated cytotoxicity can be regulated by p53 tumor suppressor gene activity in vitro.' Biol Cell **84**(3): 175-85.
- Mallet, A. I. and F. M. Cunningham (1985). 'Structural identification of platelet activating factor in psoriatic scale.' Biochem Biophys Res Commun **126**(1): 192-8.
- Manggau, M., D. S. Kim, et al. (2001). '1Alpha,25-dihydroxyvitamin D3 protects human keratinocytes from apoptosis by the formation of sphingosine-1-phosphate.' J Invest Dermatol **117**(5): 1241-9.
- Mangold, H. K. and N. Weber (1987). 'Biosynthesis and biotransformation of ether lipids.' Lipids **22**(11): 789-99.
- Manser, E., T. Leung, et al. (1994). 'A brain serine/threonine protein kinase activated by Cdc42 and Rac1.' Nature **367**(6458): 40-6.
- Martel, V., C. Racaud-Sultan, et al. (2001). 'Conformation, localization, and integrin binding of talin depend on its interaction with phosphoinositides.' J Biol Chem **276**(24): 21217-27.
- Marzio, R., J. Mauel, et al. (1999). 'CD69 and regulation of the immune function.' Immunopharmacol Immunotoxicol **21**(3): 565-82.
- Matzke, A., U. Massing, et al. (2001). 'Killing tumour cells by alkylphosphocholines: evidence for involvement of CD95.' Eur J Cell Biol **80**(1): 1-10.
- Maurer, H. R. and P. Hilgard (1992). 'Induction of tumor cell differentiation by alkylphosphocholines: a new approach for in vitro screening.' Prog Exp Tumor Res **34**: 90-7.
- May, G. L., L. C. Wright, et al. (1988). 'Plasma membrane lipid composition of vinblastine sensitive and resistant human leukaemic lymphoblasts.' Int J Cancer **42**(5): 728-33.
- McMillan, J. R., M. Akiyama, et al. (2003). 'Epidermal basement membrane zone components: ultrastructural distribution and molecular interactions.' J Dermatol Sci **31**(3): 169-77.
- McMullan, R., S. Lax, et al. (2003). 'Keratinocyte differentiation is regulated by the Rho and ROCK signaling pathway.' Curr Biol **13**(24): 2185-9.

- Mease, P. J. (2005). 'Psoriatic arthritis therapy advances.' Curr Opin Rheumatol **17**(4): 426-32.
- Mende, S., E. Teuscher, et al. (1989). 'The effect of alkyl-lysophospholipids and membrane potentials, proliferation and migration of isolated calf aorta endothelial cells.' Pharmazie **44**(10): 713-5.
- Mercurio, A. M., I. Rabinovitz, et al. (2001). 'The alpha 6 beta 4 integrin and epithelial cell migration.' Curr Opin Cell Biol **13**(5): 541-5.
- Michel, L., Y. Denizot, et al. (1990). 'Production of paf-acether by human epidermal cells.' J Invest Dermatol **95**(5): 576-81.
- Mickeleit M., T. Wieder et al. (1998). 'A Glucose-Containing Ether Lipid (Glc-PAF) as an Antiproliferative Analogue of the Platelet-Activating Factor.' Angew. Chem. Int. Ed. **37**(3):351-53.
- Mickeleit M., T. Wieder, et al. (1995). 'Glc-PC, a New Type of Glucosidic Phospholipid.' Angew. Chem. Int. Ed. **34**(23/24):2667-69.
- Moestrup, S. K. and H. J. Moller (2004). 'CD163: a regulated hemoglobin scavenger receptor with a role in the anti-inflammatory response.' Ann Med **36**(5): 347-54.
- Mollinedo, F., J. L. Fernandez-Luna, et al. (1997). 'Selective induction of apoptosis in cancer cells by the ether lipid ET-18-OCH₃ (Edelfosine): molecular structure requirements, cellular uptake, and protection by Bcl-2 and Bcl-X(L).' Cancer Res **57**(7): 1320-8.
- Moolenaar, W. H. (1999). 'Bioactive lysophospholipids and their G protein-coupled receptors.' Exp Cell Res **253**(1): 230-8.
- Munder, P. G. and O. Westphal (1990). 'Antitumoral and other biomedical activities of synthetic ether lysophospholipids.' Chem Immunol **49**: 206-35.
- Murray, H. W. and S. Delph-Etienne (2000). 'Visceral leishmanicidal activity of hexadecylphosphocholine (miltefosine) in mice deficient in T cells and activated macrophage microbial mechanisms.' J Infect Dis **181**(2): 795-9.
- Nemes, Z., L. N. Marekov, et al. (1999). 'Involucrin cross-linking by transglutaminase 1. Binding to membranes directs residue specificity.' J Biol Chem **274**(16): 11013-21.
- Nicoletti, I., G. Migliorati, et al. (1991). 'A rapid and simple method for measuring thymocyte apoptosis by propidium iodide staining and flow cytometry.' J Immunol Methods **139**(2): 271-9.
- Ninio, E. (2005). 'Phospholipid mediators in the vessel wall: involvement in atherosclerosis.' Curr Opin Clin Nutr Metab Care **8**(2): 123-31.

- Nixon, D. F., E. M. Aandahl, et al. (2005). 'CD4(+)CD25(+) regulatory T cells in HIV infection.' Microbes Infect.
- Noh, D. Y., S. H. Shin, et al. (1995). 'Phosphoinositide-specific phospholipase C and mitogenic signaling.' Biochim Biophys Acta **1242**(2): 99-113.
- Noseda, A., J. G. White, et al. (1989). 'Membrane damage in leukemic cells induced by ether and ester lipids: an electron microscopic study.' Exp Mol Pathol **50**(1): 69-83.
- Nyquist, D. A., I. Watanabe, et al. (1992). 'Alkyllysophospholipid influenced melanoma cell morphology is associated with decreased attachment to basement membrane.' Ukr Biokhim Zh **64**(3): 76-85.
- O'Connor, K. L., B. K. Nguyen, et al. (2000). 'RhoA function in lamellae formation and migration is regulated by the alpha6beta4 integrin and cAMP metabolism.' J Cell Biol **148**(2): 253-8.
- O'Toole, E. A., M. P. Marinkovich, et al. (1997). 'Laminin-5 inhibits human keratinocyte migration.' Exp Cell Res **233**(2): 330-9.
- Oberle, C., U. Massing, et al. (2005). 'On the mechanism of alkylphosphocholine (APC)- induced apoptosis in tumour cells.' Biol Chem **386**(3): 237-45.
- Okkenhaug, K. and B. Vanhaesebroeck (2001). 'New responsibilities for the PI3K regulatory subunit p85 alpha.' Sci STKE 2001(65): PE1.
- Omelchenko, T., J. M. Vasiliev, et al. (2003). 'Rho-dependent formation of epithelial 'leader' cells during wound healing.' Proc Natl Acad Sci USA **100**(19): 10788-93.
- Owens, D. M. and F. M. Watt (2003). 'Contribution of stem cells and differentiated cells to epidermal tumours.' Nat Rev Cancer **3**(6): 444-51.
- Palmblad, J., J. Samuelsson, et al. (1990). 'Interactions between alkylglycerols and human neutrophil granulocytes.' Scand J Clin Lab Invest **50**(4): 363-70.
- Papp, H., G. Czifra, et al. (2003). 'Protein kinase C isozymes regulate proliferation and high cell density-mediated differentiation in HaCaT keratinocytes.' Exp Dermatol **12**(6): 811-24.
- Pawelczyk, T. and J. M. Lowenstein (1993). 'Inhibition of phospholipase C delta by hexadecylphosphorylcholine and lysophospholipids with antitumor activity.' Biochem Pharmacol **45**(2): 493-7.
- Pei, Y., L. A. Barber, et al. (1998). 'Activation of the epidermal platelet-activating factor receptor results in cytokine and cyclooxygenase-2 biosynthesis.' J Immunol **161**(4): 1954-61.

Peiser, L. and S. Gordon (2001). 'The function of scavenger receptors expressed by macrophages and their role in the regulation of inflammation.' Microbes Infect **3**(2): 149-59.

Perez-Victoria, J. M., F. J. Perez-Victoria, et al. (2001). 'Alkyl-lysophospholipid resistance in multidrug-resistant Leishmania tropica and chemosensitization by a novel P-glycoprotein-like transporter modulator.' Antimicrob Agents Chemother **45**(9): 2468- 74.

Petersen, E. S., E. E. Kelley, et al. (1992). 'Membrane lipid modification and sensitivity of leukemic cells to the thioether lipid analogue BM 41.440.' Cancer Res **52**(22): 6263- 9.

Pignol, B., S. Chaumeron, et al. (1992). 'Immunomodulatory activity of two new aza alkyl phospholipid antineoplastic drugs.' Anticancer Drugs **3**(6): 599-608.

Pitton, C., M. Lanson, et al. (1989). 'Presence of PAF-acether in human breast carcinoma: relation to axillary lymph node metastasis.' J Natl Cancer Inst **81**(17): 1298-302.

Plotzke, K. P., T. Haradahira, et al. (1992). 'Selective localization of radioiodinated alkylphosphocholine derivatives in tumors.' Int J Rad Appl Instrum B **19**(7): 765-73.

Ponec, M., A. Weerheim, et al. (1988; A). 'Proliferation and differentiation of human squamous carcinoma cell lines and normal keratinocytes: effects of epidermal growth factor, retinoids, and hydrocortisone.' In Vitro Cell Dev Biol **24**(8): 764-70.

Ponec, M., A. Weerheim, et al. (1988; B). 'Lipid composition of cultured human keratinocytes in relation to their differentiation.' J Lipid Res **29**(7): 949-61.

Ponec, M., A. Weerheim, et al. (1989). 'Differentiation of cultured human keratinocytes: effect of culture conditions on lipid composition of normal vs. malignant cells.' In Vitro Cell Dev Biol **25**(8): 689-96.

Powis, G. (1992). 'Drugs active against growth factor and oncogene phosphatidylinositol signalling pathways.' Semin Cancer Biol **3**(6): 343-50.

Powis, G., M. J. Seewald, et al. (1992). 'Selective inhibition of phosphatidylinositol phospholipase C by cytotoxic ether lipid analogues.' Cancer Res **52**(10): 2835-40.

Prescott, S. M., G. A. Zimmerman, et al. (2000). 'Platelet-activating factor and related lipid mediators.' Annu Rev Biochem **69**: 419-45.

Principe, P., H. Coulomb, et al. (1992; A). 'Evaluation of combinations of antineoplastic ether phospholipids and chemotherapeutic drugs.' Anticancer Drugs **3**(6): 577-87.

- Principe, P., C. Sidoti, et al. (1992; B). 'Tumor cell kinetics following antineoplastic ether phospholipid treatment.' Cancer Res **52**(9): 2509-15.
- Pushkareva, M. Y., A. S. Janoff, et al. (1999). 'Inhibition of cell division but not nuclear division by 1-O- octadecyl-2-O-methyl-Sn-glycero-3-phosphocholine.' Cell Biol Int. **23**(12):817-28
- Rabinovitz, I. and A. M. Mercurio (1996). 'The integrin alpha 6 beta 4 and the biology of carcinoma.' Biochem Cell Biol **74**(6): 811-21.
- Raghavan, S. and J. Holmgren (2005). 'CD4(+)CD25(+) suppressor T cells regulate pathogen induced inflammation and disease.' FEMS Immunol Med Microbiol **44**(2): 121-7.
- Rand, J. H. (2002). 'Molecular pathogenesis of the antiphospholipid syndrome.' Circ Res **90**(1): 29-37.
- Reed, C. B., W. Tang, et al. (1991). 'Antineoplastic ether-linked phospholipid induces differentiation of acute myelogenous leukemic KG-1 cells into macrophage-like cells.' Life Sci **49**(17): 1221-7.
- Reman, F. C., R. A. Demel, et al. (1969). 'Studies on the lysis of red cells and bimolecular lipid leaflets by synthetic lysolecithins, lecithins and structural analogs.' Chem Phys Lipids **3**(3): 221-33.
- Rice, R. H. and H. Green (1978). 'Relation of protein synthesis and transglutaminase activity to formation of the cross-linked envelope during terminal differentiation of the cultured human epidermal keratinocyte.' J Cell Biol **76**(3): 705-11.
- Ridley, A. J., M. A. Schwartz, et al. (2003). 'Cell migration: integrating signals from front to back.' Science **302**(5651): 1704-9.
- Ritter, M., C. Buechler, et al. (1999). 'The scavenger receptor CD163: regulation, promoter structure and genomic organization.' Pathobiology **67**(5-6): 257-61.
- Roos, G. and W. E. Berdel (1986). 'Sensitivity of human hematopoietic cell lines to an alkyl- lysophospholipid-derivative.' Leuk Res **10**(2): 195-202.
- Rossi, A., S. I. Jang, et al. (1998). 'Effect of AP1 transcription factors on the regulation of transcription in normal human epidermal keratinocytes.' J Invest Dermatol **110**(1): 34- 40.
- Rudolph, R., E. Kownatzki (2004). 'Corneometric, sebumetric and TEWL measurements following the cleaning of atopic skin with a urea emulsion versus a detergent cleanser.' Contact Dermatitis **50**(6):354-8.
- Ruggeri, Z. M. (2002). 'Platelets in atherothrombosis.' Nat Med **8**(11): 1227-34.

- Ruiter, G. A., M. Verheij, et al. (2001). 'Alkyl-lysophospholipids as anticancer agents and enhancers of radiation-induced apoptosis.' Int J Radiat Oncol Biol Phys **49**(2): 415-9.
- Ruiter, G. A., S. F. Zerp, et al. (2003). 'Anti-cancer alkyl-lysophospholipids inhibit the phosphatidylinositol 3-kinase-Akt/PKB survival pathway.' Anticancer Drugs **14**(2): 167-73.
- Sadtler, V. M., P. Imbert, et al. (2002). 'Ostwald ripening of oil-in-water emulsions stabilized by phenoxy-substituted dextrans.' J Colloid Interface Sci **254**(2): 355-61.
- Salari, H., P. Dryden, et al. (1992; A). 'Inhibition of protein kinase C by ether-linked lipids is not correlated with their antineoplastic activity on WEHI-3B and R6X-B15 cells.' Biochim Biophys Acta **1134**(1): 81-8.
- Salari, H., P. Dryden, et al. (1992; B). 'Two different sites of action for platelet activating factor and 1-O-alkyl-2-O-methyl-sn-glycero-3-phosphocholine on platelets and leukemic cells.' Biochem Cell Biol **70**(2): 129-35.
- Samadder, P. and G. Arthur (1999). 'Decreased sensitivity to 1-O-octadecyl-2-O-methyl-glycerophosphocholine in MCF-7 cells adapted for serum-free growth correlates with constitutive association of Raf-1 with cellular membranes.' Cancer Res **59**(19): 4808- 15.
- Sancho, D., M. Gomez, et al. (2005). 'CD69 is an immunoregulatory molecule induced following activation.' Trends Immunol **26**(3): 136-40.
- Santoro, M. M. and G. Gaudino (2005). 'Cellular and molecular facets of keratinocyte reepithelialization during wound healing.' Exp Cell Res **304**(1): 274-86.
- Sato, S., K. Kume, et al. (1999). 'Accelerated proliferation of epidermal keratinocytes by the transgenic expression of the platelet-activating factor receptor.' Arch Dermatol Res **291**(11): 614-21.
- Schallier, D. C., E. A. Bruyneel, et al. (1991). 'Antiinvasive activity of hexadecylphosphocholine in vitro.' Anticancer Res **11**(3): 1285-92.
- Scherberich, J. E. (2003). 'Proinflammatory blood monocytes: main effector and target cells in systemic and renal disease; background and therapeutic implications.' Int J Clin Pharmacol Ther **41**(10): 459-64.
- Schön, M., M. P. Schön et al. (1996). 'Cell-Matrix interactions of normal and transformed human keratinocytes in vitro are modulated by the synthetic phospholipid analogue hexadecylphosphocholine.' Br J Dermatol **135**:696-701.

- Shimada, A., Y. Ota, et al. (1998). 'In situ expression of platelet-activating factor (PAF)- receptor gene in rat skin and effects of PAF on proliferation and differentiation of cultured human keratinocytes.' J Invest Dermatol **110**(6): 889-93.
- Shindou, H., S. Ishii, et al. (2000). 'Roles of cytosolic phospholipase A(2) and platelet-activating factor receptor in the Ca-induced biosynthesis of PAF.' Biochem Biophys Res Commun **271**(3): 812-7.
- Sidoti, C., P. Principe, et al. (1992). 'Cytostatic activity of new synthetic anti-tumor aza- alkyllysophospholipids.' Int J Cancer **51**(5): 712-7.
- Smith, T. A., S. Eccles, et al. (1991). 'The phosphocholine and glycerophosphocholine content of an oestrogen-sensitive rat mammary tumour correlates strongly with growth rate.' Br J Cancer **64**(5): 821-6.
- Snyder, F., T. C. Lee, et al. (1989). 'Platelet-activating factor and related ether lipid mediators. Biological activities, metabolism, and regulation.' Ann NY Acad Sci **568**: 35-43.
- Sobottka, S. B., M. R. Berger, et al. (1993). 'Structure-activity relationships of four anti-cancer alkylphosphocholine derivatives in vitro and in vivo.' Int J Cancer **53**(3):418-25.
- Soldi, R., F. Sanavio, et al. (1996). 'Platelet-activating factor (PAF) induces the early tyrosine phosphorylation of focal adhesion kinase (p125FAK) in human endothelial cells.' Oncogene **13**(3): 515-25.
- Southall, M. D., J. S. Isenberg et al. (2001). 'The platelet-activating factor receptor protects epidermal cells from tumor necrosis factor (TNF) alpha and TNF-related apoptosis-inducing ligand-induced apoptosis through an NF-kappa B-dependent process.' J Biol Chem **276**(49):45548-54.
- Stafforini, D. M., T. M. McIntyre, et al. (2003). 'Platelet-activating factor, a pleiotrophic mediator of physiological and pathological processes.' Crit Rev Clin Lab Sci **40**(6): 643-72.
- Storme, G. A., W. E. Berdell, et al. (1985). 'Antiinvasive effect of racemic 1-O-octadecyl-2- O-methylglycero-3-phosphocholine on MO4 mouse fibrosarcoma cells in vitro.' Cancer Res **45**(1): 351-7.
- Strannegard, O. and G. Roupe (1976). 'Adjuvant effect of lysolecithin analogues on the development of contact sensitivity in mice.' Int Arch Allergy Appl Immunol **51**(2): 198-205.
- Strum, J. C., A. B. Nixon, et al. (1993). 'Evaluation of phospholipase C and D activity in stimulated human neutrophils using a phosphono analog of choline phosphoglyceride.' Biochim Biophys Acta **1169**(1): 25-9.

- Tadros, T., P. Izquierdo, et al. (2004). 'Formation and stability of nano-emulsions.' Adv Colloid Interface Sci **108-109**: 303-18.
- Tarnowski, G. S., I. M. Mountain, et al. (1978). 'Effect of lysolecithin and analogs on mouse ascites tumors.' Cancer Res **38**(2): 339-44.
- Tertoolen, L. G., J. Kempenaar, et al. (1988). 'Lateral mobility of plasma membrane lipids in normal and transformed keratinocytes.' Biochem Biophys Res Commun **152**(2): 491- 6.
- Thivierge, M., J. L. Parent, et al. (1996). 'Modulation of human platelet-activating factor receptor gene expression by protein kinase C activation.' J Immunol **157**(10): 4681-7.
- Tjoelker, L. W., C. Wilder, et al. (1995). 'Anti-inflammatory properties of a platelet-activating factor acetylhydrolase.' Nature **374**(6522): 549-53.
- Tolias, K. F., L. C. Cantley, et al. (1995). 'Rho family GTPases bind to phosphoinositide kinases.' J Biol Chem **270**(30): 17656-9.
- Tsuji, T., T. Ishizaki, et al. (2002). 'ROCK and mDia1 antagonize in Rho-dependent Rac activation in Swiss 3T3 fibroblasts.' J Cell Biol **157**(5): 819-30.
- Unger, C., H. Eibl, et al. (1988). 'Hexadecylphosphocholine (D 18506) in the topical treatment of skin metastases: a phase-I trial.' Onkologie **11**(6): 295-6.
- Unger, C., W. Damenz, et al. (1989). 'Hexadecylphosphocholine, a new ether lipid analogue. Studies on the antineoplastic activity in vitro and in vivo.' Acta Oncol **28**(2): 213-7.
- Unger, C., E. Fleer, et al. (1991). 'Hexadecylphosphocholine: determination of serum concentrations in rats.' J Lipid Mediat **3**(1): 71-8.
- Unger, C., E. A. Fleer, et al. (1992; A). 'Antitumoral activity of alkylphosphocholines and analogues in human leukemia cell lines.' Prog Exp Tumor Res **34**: 25-32.
- Unger, C., H. Sindermann, et al. (1992; B). 'Hexadecylphosphocholine in the topical treatment of skin metastases in breast cancer patients.' Prog Exp Tumor Res **34**: 153-9.
- Unger, C. and H. Eibl (2001). '[Drug development from phospholipids]' Onkologie **24** Suppl 1: 18-23.
- Vagnetti, D., A. Mancini, et al. (1990). 'Effect of alkyl-lysophospholipid analogs on the morphology of a murine lymphoma cell line.' J Submicrosc Cytol Pathol **22**(3): 415- 24.

van Blitterswijk, W. J., H. Hilkmann, et al. (1987; A). 'Accumulation of an alkyl lysophospholipid in tumor cell membranes affects membrane fluidity and tumor cell invasion.' Lipids **22**(11): 820-3.

van Blitterswijk, W. J., R. L. van der Bend, et al. (1987; B). 'A metabolite of an antineoplastic ether phospholipid may inhibit transmembrane signalling via protein kinase C.' Lipids **22**(11): 842-6.

van Blitterswijk, W. J., B. W. van der Meer, et al. (1987; C). 'Quantitative contributions of cholesterol and the individual classes of phospholipids and their degree of fatty acyl (un)saturation to membrane fluidity measured by fluorescence polarization.' Biochemistry **26**(6): 1746-56.

van der Bend, R. L., J. de Widt, et al. (1992). 'The biologically active phospholipid, lysophosphatidic acid, induces phosphatidylcholine breakdown in fibroblasts via activation of phospholipase D. Comparison with the response to endothelin.' Biochem J **285** (Pt 1): 235-40.

van der Luit, A. H., M. Budde, et al. (2003). 'Different modes of internalization of apoptotic alkyl-lysophospholipid and cell-rescuing lysophosphatidylcholine.' Biochem J **374**(Pt 3): 747-53.

van der Sanden, M. H., M. Houweling, et al. (2004). 'Inhibition of phosphatidylcholine synthesis is not the primary pathway in hexadecylphosphocholine-induced apoptosis.' Biochim Biophys Acta **1636**(2-3):99-107.

Verweij, J., A. Planting, et al. (1992). 'A dose-finding study of miltefosine (hexadecylphosphocholine) in patients with metastatic solid tumours.' J Cancer Res Clin Oncol **118**(8): 606-8.

Vichi, P. and T. R. Tritton (1989). 'Stimulation of growth in human and murine cells by adriamycin.' Cancer Res **49**(10): 2679-82.

Vogler, W. R. (1988). 'Acute myelogenous leukemia: problems in the elderly patient.' Keio J Med **37**(2): 122-31.

Volc-Platzer, B., O. Majdic, et al. (1984). 'Evidence of HLA-DR antigen biosynthesis by human keratinocytes in disease.' J Exp Med **159**(6): 1784-9.

Volk, H. D., S. R. Waschke, et al. (1985). 'Decrease of HLA-DR antigen expression by human monocytes during cultivation in absence of exogenous or endogenous interferon-gamma.' Immunol Lett **10**(2): 103-7.

Wakita, H., Y. Tokura, et al. (1994). 'Keratinocyte differentiation is induced by cell-permeant ceramides and its proliferation is promoted by sphingosine.' Arch Dermatol Res **286**(6): 350-4.

Wang, S. and L. Chen (2004). 'Co-signaling molecules of the B7-CD28 family in positive and negative regulation of T lymphocyte responses.' Microbes Infect **6**(8): 759-66.

Wang, X. Q., P. Sun, et al. (2001). 'Inhibition of integrin-linked kinase/protein kinase B/Akt signaling: mechanism for ganglioside-induced apoptosis.' J Biol Chem **276**(48): 44504-11.

Webb, D. J., J. T. Parsons, et al. (2002). 'Adhesion assembly, disassembly and turnover in migrating cells – over and over and over again.' Nat Cell Biol **4**(4): E97-100.

Webb, D. J., K. Donais, et al. (2004). 'FAK-Src signalling through paxillin, ERK and MLCK regulates adhesion disassembly.' Nat Cell Biol **6**(2): 154-61.

Weber, N. and H. Benning (1988). 'Metabolism of ether glycolipids with potentially antineoplastic activity by Ehrlich ascites tumor cells.' Biochim Biophys Acta **959**(1): 91-4.

Weerheim, A. and M. Ponec (2001). 'Determination of stratum corneum lipid profile by tape stripping in combination with high-performance thin-layer chromatography.' Arch Dermatol Res **293**(4): 191-9.

Wells, A. (2000). 'Tumor invasion: role of growth factor-induced cell motility.' Adv Cancer Res **78**: 31-101.

Whittard, J. D. and S. K. Akiyama (2001). 'Activation of beta1 integrins induces cell-cell adhesion.' Exp Cell Res **263**(1): 65-76.

Wieder, T., Z. Zhang, et al. (1996). 'The antitumor phospholipid analog, hexadecylphosphocholine, activates cellular phospholipase D.' Cancer Lett **100**(1-2): 71-9.

Wieder, T., C. E. Orfanos, et al. (1998). 'Induction of ceramide-mediated apoptosis by the anticancer phospholipid analog, hexadecylphosphocholine.' J Biol Chem **273**(18): 11025-31.

Wiese, A., T. Wieder, et al. (2000). 'Structure-dependent effects of glucose-containing analogs of platelet activating factor (PAF) on membrane integrity.' Biol Chem **381**(2): 135-44.

Wirtz, K. W. (1991). 'Phospholipid transfer proteins.' Annu Rev Biochem **60**: 73-99.

Woodley, D. T., D. C. Chen, et al. (1993). 'Re-epithelialization. Human keratinocyte locomotion.' Dermatol Clin **11**(4):641-6.

Wu, H., C. Ramachandran, et al. (2001). 'Topical transport of hydrophilic compounds using water-in-oil nanoemulsions.' Int J Pharm **220**(1-2): 63-75.

Yong P., L. A. Barber, et al. (1998). 'Activation of the epidermal platelet-activating factor receptor results in cytokine in cyclooxygenase-2 biosynthesis.'

Zhang, K. and R. H. Kramer (1996). 'Laminin 5 deposition promotes keratinocyte motility.' Exp Cell Res **227**(2): 309-22.

Zheng, M. and U. Mrowietz (1997). 'Phenotypic differences between human blood monocyte subpopulations in psoriasis and atopic dermatitis.' J Dermatol **24**(6): 370-8.

Zhou, X., X. Lu, et al. (1996). '1-O-octadecyl-2-O-methyl-glycerophosphocholine inhibits the transduction of growth signals via the MAPK cascade in cultured MCF-7 cells.' J Clin Invest **98**(4): 937-44.

Zola, H. (2000). 'Markers of cell lineage, differentiation and activation.' J Biol Regul Homeost Agents **14**(3): 218-9.

16 Veröffentlichungen

Veröffentlichungen

The ether lipid, Inositol-C2-PAF, is a potent Inhibitor of Cell Proliferation in HaCaT Cells
A. Fischer, D. Müller, M. Zimmermann-Kordmann, B. Kleuser, M. Mickeleit, S. Laabs, W. Löwe, W. Reutter and K. Danker
ChemBioChem, in press 2005

Glucosamine-Glycerophospholipids activate cell matrix adhesion and migration
T. Bartholmäus, T. Heyn, M. Mickeleit, A. Fischer, W. Reutter and K. Danker
J Med Chem, 48 (21), 6750-6755, 2005

Buchbeiträge

Modified and modifying sugars as a new tool for the development of therapeutic agents -
Glycosidated phospholipids as a new tool of antiproliferative reagents
K. Danker, A. Fischer, W. Reutter; Ed. C.H. Wong

Kurz- und Posterbeiträge

Jahrbuch 2002 des Fachbereichs Humanmedizin des Universitätsklinikums Benjamin Franklin der Freien Universität Berlin

A novel glycosidic phospholipid, inositol-PAF, inhibits cells proliferation and activates cell matrix adhesion of HaCaT cells

A. Fischer, T. Heyn, S. Laabs, W. Reutter and K. Danker

European Life Science Organisation Meeting, Nizza, 2002

Influence of a novel group of Alkyl-ether-lipids on HaCaT cells

A. Fischer, T. Heyn, M. Mickeleit, S. Laabs, W. Reutter and K. Danker

Jahrbuch 2003 Charité - Universitätsmedizin Berlin Campus Benjamin Franklin

The phospholipid analog Inositol-PAF is a potent inhibitor of cell proliferation and influences cell matrix adhesion of HaCaT cells

A. Fischer, M. Zimmermann-Kordmann, S. Laabs, P. Daniel, W. Mehnert, W. Reutter and K. Danker

Kongreß der Gesellschaft für Biochemie und Molekularbiologie, Bonn, 2003

Influence of a novel group of Alkyl-ether-lipids on matrix-adhesion HaCaT cells

A. Fischer, T. Heyn, M. Mickeleit, S. Laabs, W. Reutter and K. Danker

29th congress of the federation of European Biochemical Societies and FEBS FORUM FOR YOUNG SCIENTISTS, Warschau, 2004

Ino-PAF inhibits cell proliferation of HaCaT-cells and induces terminal differentiation

A. Fischer, S. Laabs, M. Zimmermann-Kordmann, W. Reutter and K. Danker

Meeting: Targets, Drugs and Carriers - Novel Therapeutic Approaches, Berlin-Dahlem, 2004

Ino-PAF inhibits cell proliferation of HaCaT-cells and induces terminal differentiation

A. Fischer, S. Laabs, M. Zimmermann-Kordmann, W. Reutter and K. Danker

Adhesion meeting 2005; podosomes - invadopodia - focal adhesion, München

The alkyl-ether-lipid Inositol-C2-PAF influences matrix-adhesion and migration of HaCaT- and SCC-25-cells

A. Fischer, W. Reutter and K. Danker

17 Lebenslauf

Annette Fischer

geboren am 23.11.1974 in Dresden

1980-1989 Polytechnische Oberschule Richard Neubert, Dresden

1989-1991 Mittlere Reife
Polytechnische Oberschule Kurt Aehlig, Dresden

1991-1992 Rotary Schüler-Austausch
Riverside Girls Highschool, Sydney, Australien

1992-1994 Abitur
Bertold Brecht Gymnasium, Dresden

1994-1995 Auslandsaufenthalt Australien

1995-2000 Studium der Pharmazie, 2. Staatsexamen
Freie Universität Berlin

2000-2001 Praktisches Jahr, Approbation als Apotheker
Schering AG, Suarez-Apotheke

seit 2001 Doktorarbeit am Institut für Biochemie und Molekularbiologie
Charité - Universitätsmedizin Berlin, Campus Benjamin Franklin

18 Danksagung

Ich danke ganz herzlich Privatdozentin Dr. Kerstin Danker für die Vergabe des Themas, für ihre ermutigende, engagierte Unterstützung meiner Arbeit und die Möglichkeit, wissenschaftliche Selbständigkeit zu lernen.

Frau Professor Monika Schäfer-Korting danke ich für ihre Bereitschaft, diese Arbeit zu begutachten und für die gute Zusammenarbeit mit ihrer Arbeitsgruppe.

Herrn Professor Werner Reutter danke ich für die Förderung meiner Arbeit, sowie ich mich bei den Arbeitsgruppen von PD Dr. Hua Fan, PD Dr. Stephan Hinderlich, PD Dr. Lothar Lucka und PD Dr. Rüdiger Horstkorte für die gute Zusammenarbeit, die offene und kritische Arbeitsatmosphäre bedanke.

Zugleich möchte ich mich bei Dr. Burkhard Kleuser, Dr. Wolfgang Mehnert und Prof. Klaus Kramer und ihren Mitarbeitern für die technische Unterstützung und die gelungenen Kooperationen bedanken.

Dr. Martin Zimmermann-Kordmann und Detlef Grunow danke ich für die Durchführung der MALDI-TOF-MS Analysen.

Werner Hofmann danke ich für seine zuverlässige Hilfe bei den proteinchemischen Versuchen.

Ich danke den Mitgliedern des Mädchenzimmers (Nadja, Diana, Kerstin, Wenke, Stephanie) und allen anderen Mitarbeitern für die angenehmen Seiten des Laborlebens und die gemeinsamen Unternehmungen, besonders Skipper Astrid, Mitsegler Verena und Kirstin.

Besonders danke ich Thomas Hildmann, dessen Zuspruch, technische Hilfe und Geduld, mir die Kraft gab, schwierige Phasen während dieser Arbeit zu überwinden.

Abschließend möchte ich mich bei meinen Eltern und Brüdern bedanken, die mich gefördert und geprägt haben.