

CURRICULUM VITAE



**Prof. Manfred Schmitt, Dr. rer. nat., Dr. med. habil.
(Ph. D., M. D. sci.), Dipl.-Biologist**

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Born on September 7, 1947, Nordenham, Germany.
Married to Elisabeth Schmitt, one daughter, Michaela, born 1979.

University studies and positions

- 1969-1978** Studies in chemistry, biology and biochemistry, University of Mainz, Germany
1974-1977 Graduate student, Ph. D. (Dept. Biochemistry, University of Mainz, Germany)
1975 Diploma in biology (Dept. Biochemistry, University of Mainz, Germany)
1976 Certificate to teach chemistry and biology; Senior High School (*Gymnasium*). (University of Mainz, Germany)
1978 Ph. D. in biochemistry (Dept. Biochemistry, University of Mainz, Germany, magna cum laude)
1978-1981 Assistant Professor (Dept. Med. Microbiology, University of Mainz, Germany)
1981-1983 Visiting Investigator (Scripps Clinic and Research Foundation, Dept. Immunopathology, La Jolla, California, USA, with Prof. Dr. Charles Cochrane)
1983-1987 Associate Professor (Dept. Pathology, University of Berne, Switzerland)
1987-1993 Associate Professor and Director of Clinical Research Unit (Department of Obstetrics & Gynecology, Klinikum rechts der Isar, Technical University of Munich, Germany)
1989 Habilitation and Privatdozent (Dr. med. habil. = Dr. med. sci.) in Experimental Gynecology, Technical University of Munich
1993-today Full Professor (C3) of Experimental Gynecology and Director of Clinical Research Unit (Department of Obstetrics & Gynecology, Klinikum rechts der Isar, Technical University of Munich, Germany)

Previous and present areas of research:

- 1974-1977** Department of Biochemistry, University of Mainz, Germany:
Investigations of structural, kinetic, and immunological parameters of membrane-associated Me^{2+} -ATPases of eukaryotic and prokaryotic cells.
- 1978-1980** Department of Medical Microbiology, University of Mainz, Germany:
Analysis of structural/kinetic parameters of complement-dependent receptor systems.
- 1981-1983** Department of Immunopathology, Scripps Clinic and Research Foundation, La Jolla, California, USA:
Characterization/identification of receptor systems in inflammation and chemotaxis.
- 1983-1987** Department of Pathology, University of Berne, Switzerland:
Chemotaxis and investigation of signal-transduction pathways in phagocytic cells.
- 1987-today** Department of Obstetrics & Gynecology, Technical University of Munich, Germany:
Tumor-associated proteolysis related to tumor cell dissemination and metastasis. Metastasis research using tumor-bearing mice and transgenic mice. Proteases as novel antimetastatic targets. Biomarkers and prognostic as well as predictive factors in solid malignant tumors (e.g. breast, ovary, gastrointestinal tract, etc). Signal transduction pathways, cell biology of tumor cell surface receptors and integrins. Structure/function relation of receptor-ligand systems (e.g. uPA-system). Somatic gene therapy applying viral and liposomal vectors. Tumor tissue gene analysis including mRNA-expression and DNA-methylation profiling. Immunohistochemical and proteomic analysis of tumor-associated biomarkers. uPAR-Interactome analysis. Biosensors. Tumor banking.

Major research grants by: Swiss National Foundation (Nationalfond), Rolex-Fond, DFG (Postdoc research grant [Ausbildungsstipendium] USA, Clinical Research Unit GR280, Graduate Consortium (Graduierten-Kolleg 333), Focal Research Program (Schwerpunktprogramm) 1100, Special Research Center (Sonderforschungsbereich) SFB 207, SFB 456, SFB 469, German Research Ministry (Bundesforschungsministerium BMBF), German Ministry of Economics (Bundwirtschaftsministerium BMWi) BIOREGIO-M, Wilhelm-Sander-Foundation, German Cancer Aid (Krebshilfe, Dr. Mildred Scheel-Stiftung), Special University Research Program (Hochschulsonderprogramm HSP Bayern), Commission for Clinical Research (Kommission Klinische Forschung) TU München, European Union Funding (BIOMED-1,

BIOMED-2, 4th Medical and Health Program, PECO, Esprit-3, TMR, Marie-Curie-Programm, 6th Framework Program, 7th Framework Program), IUCC, DAAD, Bavarian Research Foundation (Bayerische Forschungsstiftung [FORTEPRO], Federal Institute for Drugs and Medical Devices (Bundesinstitut für Arzneimittel und Medizinprodukte [BfArM]), European Organization for Research and Treatment of Cancer (EORTC) Translational Research Fund, Research networks with pharmaceutical companies.

Doctoral theses and habilitations: In charge of 190 dissertations and 17 habilitations.

Teaching: Bachelor program, Master program, PhD program, MD PhD program, institutional research seminars, courses in cancer biology, oncology, cancer biomarkers.

Patents: 72 patents/patent applications.

Conference organization: (Co-)organizer of 38 national/international conferences.

Co-editor of journals: Thrombosis and Haemostasis, European Journal of Cancer, International Journal of Oncology, Cancer Therapy, Critical Reviews in Clinical Laboratory Science, The Open Clinical Chemistry Journal, Journal of Clinical Proteomics, Thrombosis Research (terminated).

Expert reviews for several international scientific journals and research institutions/foundations, e.g. European Commission, German Research Association, German Cancer Aid, Alexander von Humboldt-Foundation, Wilhelm Sander-Foundation, Italian, Dutch, English, American, French, Spanish research foundations.

Other experience and professional memberships and appointments

Member, American Association for Cancer Research, Philadelphia, USA

Member, International Society on Thrombosis and Haemostasis, Carrboro, USA

Member, International Society of Fibrinolysis and Proteolysis, Leuven, Belgium

Member, International Proteolysis Society, USA

Member, European Organization for Research and Treatment of Cancer (EORTC), Brussels, Belgium

Member, PathoBiology Group (EORTC), Brussels, Belgium

Member, Translational Advisory Committee and Network of Core Institutions (EORTC), Brussels, Belgium

Member, Gesellschaft fuer Biochemie und Molekularbiologie, Frankfurt, Germany

Member, Deutsche Gesellschaft fuer Zellbiologie, Heidelberg, Germany

Member, Tumor Center Munich, Germany

Member, Deutsche Krebsgesellschaft (German Cancer Association)

Member, Brustkrebs Deutschland, Munich, Germany

Member, Board, Henner Graeff Foundation, Munich, Germany

Member, Board, Frey-Werle-Foundation, Munich, Germany (from **(2014)**)

Co-founder of Wilex Biotechnology GmbH (now Wilex AG), Munich, Germany, in 1997.

Publications: 411 full publications in scientific journals and books, more than 400 presentations at meetings and institutional seminars.

Selected publications (out of 411)

- 1) Dorn J, Beaufort N, **Schmitt M**, Diamandis EP, Goettig P, Magdolen, V. **(2014)**. Function and clinical relevance of kallikrein-related peptidases and other serine proteases in gynecological cancers. *Critical Reviews in Clinical Laboratory Sciences*, Epub ahead.
- 2) Dorn J, Gkazepis A, Kotzsch M, Kremer M, Propping C, Mayer K, Mengele K, Diamandis EP, Kiechle M, Magdolen V, **Schmitt M**. **(2014)**. Clinical value of protein expression of kallikrein-related peptidase 7 (KLK7) in ovarian cancer. *Biological Chemistry* 395:95-107.
- 3) Aichler M, Elsner M, Ludyga N, Feuchtinger A, Zangen V, Maier SK, Balluff B, Schöne C, Hierber L, Braselmann H, Meding S, Rauser S, Zischka H, Aubele M, **Schmitt M**, Feith M, Hauck SM, Ueffing M, Langer R, Kuester B, Zitzelsberger H, Höfler H, Walch AK. **(2013)**. Clinical response to chemotherapy in oesophageal adenocarcinoma patients is linked to defects in mitochondria. *Journal of Pathology* 230:410-419.
- 4) Dorn J, Bayani J, Yousef GM, Yang F, Magdolen V, Kiechle M, Diamandis EP, **Schmitt M**. **(2013)**. Clinical utility of kallikrein-related peptidases (KLK) in urogenital malignancies. *Thrombosis and Haemostasis* 110:408-422.
- 5) Falkenberg N, Anastasov N, Rappl K, Braselmann H, Auer G, Walch A, Huber M, Höfig I, **Schmitt M**, Höfler H, Atkinson MJ, Aubele M. **(2013)**. miR-221/-222 differentiate prognostic groups in advanced breast cancers and influence cell invasion through uPAR. *British Journal of Cancer* 109:2714-2723.
- 6) Gross E, Meul C, Raab S, Propping C, Avril S, Aubele M, Gkazepis A, Schuster T, Grebenchtchikov N, **Schmitt M**, Kiechle M, Meijer J, Vijzelaar R, Meindl A, van Kuilenburg, A. **(2013)**. Somatic copy number changes in DPYD reflect chemosensitivity in triple-negative breast cancers. *British Journal of Cancer* 109:2347-2355.
- 7) Harbeck N, **Schmitt M**, Meisner C, Friedel C, Untch M, Schmid M, Sweep CGJ, Lisboa BW, Lux MP, Beck T, Hasmüller S, Kiechle M, Jänicke F, Thomssen C, for the Chemo-N0 Study Group. **(2013)**. Ten-year analysis

- of the prospective multicenter Chemo-N0 trial validates ASCO-recommended biomarkers uPA and PAI-1 for therapy decision making in node-negative breast cancer patients. *European Journal of Cancer* 49:1825-1835.
- 8) Ludyga N, Anastasov N, Rosemann M, Seiler J, Lohmann N, Braselmann H, Mengele K, **Schmitt M**, Höfler H, Aubele M. (2013). Effects of simultaneous knockdown of HER2 and PTK6 on malignancy and tumor progression in human breast cancer cells. *Molecular Cancer Research* 11:381-392.
 - 9) Bronger H, Kraeft S, Schwarz-Boeger U, Cerny C, Stöckel A, Avril S, Kiechle M, **Schmitt M**. (2012). Modulation of CXCR3 ligand secretion by prostaglandin E2 and cyclooxygenase inhibitors in human breast cancer. *Breast Cancer Research* 14:R30.
 - 10) Daidone MG, Foekens JA, Harbeck N, Martens J, Brünner N, Thomssen C, Hall JA, Salgado R, Dittmer J, Geurts-Moespot A, Duffy MJ, Sweep FCGJ, **Schmitt M**. (2012). Identification, validation and clinical implementation of tumor-associated biomarkers: translational strategies of the EORTC-PathoBiology Group. *Eur J Cancer Supplements* 10:120-127.
 - 11) Grismayer B, Soelch S, Seubert B, Kirchner T, Schäfer S, Baretton G, **Schmitt M**, Luther T, Krüger A, Kotzsch M, Magdolen V. (2012). Rab31 expression levels modulate tumor-relevant characteristics of breast cancer cells. *Molecular Cancer* 11:62.
 - 12) Hofer S, Mengele K, Stemmler HJ, **Schmitt M**, Pestalozzi B. (2012). Intrathecal trastuzumab: dose matters. *Acta Oncologica* 51:955-956.
 - 13) Seiz L, Dorn J, Kotzsch M, Walch A, Grebentchikov NI, Gkazepis A, Schmalfeldt B, Kiechle M, Bayani J, Diamandis EP, Langer R, Sweep FCGJ, **Schmitt M**, Magdolen V. (2012). Stromal cell-associated expression of kallikrein-related peptidase 6 (KLK6) indicates poor prognosis of ovarian cancer patients. *Biological Chemistry* 393:391-401.
 - 14) Dorn J, Harbeck N, Kates R, Gkazepis A, Scorilas A, Soosaipillai A, Diamandis E, Kiechle M, Schmalfeldt B, **Schmitt M**. (2011). Impact of expression differences of kallikrein-related peptidases and of uPA and PAI-1 between primary tumor and omentum metastasis in advanced ovarian cancer. *Annals in Oncology* 22:877-883.
 - 15) Dorn J, Magdolen V, Gkazepis A, Gerte T, Harlozinska A, Sedlaczek P, Diamandis E, P, Schuster T, Harbeck N, Kiechle M, **Schmitt M**. (2011). Circulating biomarker tissue kallikrein-related peptidase KLK5 impacts ovarian cancer patients' survival. *Annals in Oncology* 22:1783-1790.
 - 16) Hauser S, Bickel L, Weinspach D, Gerg M, Schäfer M, K, Pfeifer M, Hazin J, Schelter F, Weidle U, H, Ramser J, Volkmann J, Meindl A, **Schmitt M**, Schrötzlmair F, Altevogt P, Krüger A. (2011). Full-length L1CAM and not its $\Delta 2\Delta 27$ splice variant promotes metastasis through induction of gelatinase expression. *PLoS One*. 6:e18989.
 - 17) Kotzsch M, Dorn J, Doetzer K, Schmalfeldt B, Krol J, Baretton G, Kiechle M, **Schmitt M**, Magdolen V. (2011). mRNA expression levels of the biological factors uPAR uPAR-del4/5 and rab31 displaying prognostic value in breast cancer are not clinically relevant in advanced ovarian cancer. *Biol Chem*. 392:1047-1051.
 - 18) **Schmitt M**, Harbeck N, Brünner N, Jänicke F, Meisner C, Mühlenweg B, Jansen H, Dorn J, Nitz U, Kantelhardt E, J, Thomssen C. (2011). Review of clinical studies employing Level-of-Evidence-1 disease forecast cancer biomarkers urokinase-type plasminogen activator (uPA) and its inhibitor PAI-1. *Expert Rev Mol Diagn*. 11:617-634.
 - 19) Rauser S, Marquardt C, Balluff B, Deininger SO, Albers C, Belau E, Hartmer R, Suckau D, Specht K, Ebert MP, **Schmitt M**, Aubele M, Höfler H, Walch A. (2010). Classification of HER2 receptor status in breast cancer tissues by MALDI Imaging Mass Spectrometry. *J Proteome Res*. 9:1854-1863.
 - 20) Seiz L, Kotzsch M, Grebentchikov N, Geurts-Moespot A, Fuessel S, Goettig P, Gkazepis A, Wirth MP, **Schmitt M**, Loßnitzer A, Sweep FC, Magdolen V. (2010). Polyclonal antibodies against kallikrein-related peptidase 4 (KLK4): immunohistochemical assessment of KLK4 expression in healthy tissues and prostate cancer. *Biological Chemistry* 391:391-340.
 - 21) Lössner D, Abou-Ajram C, Bengel A, Aumercie, M, **Schmitt M**, Reuning U. (2009). Integrin $\alpha v \beta 3$ upregulates integrin-linked kinase expression in human ovarian cancer cells via enhancement of ILK gene transcription. *Journal of Cellular Physiology* 220:367-375.
 - 22) Thomssen C, Harbeck N, Dittmer J, Abraha-Spaeth S, Papendick N, Paradiso A, Lisboa B, Jaenicke F, **Schmitt M**, Vetter M. (2009). Feasibility of measuring the prognostic factors uPA and PAI-1 in core needle biopsy breast cancer specimens. *Journal of the National Cancer Institute* 101:1028-1029.
 - 23) Gluz O, Mengele K, **Schmitt M**, Kates R, Diallo-Danebrock R, Neff F, Royer HD, Eckstein N, Mohrmann S, Ting E, Kiechle M, Poremba C, Nitz U, Harbeck N. (2009). Y-Box binding protein YB-1 identifies high-risk primary breast cancer patients benefiting from rapidly cycled tandem high-dose adjuvant chemotherapy. *Journal of Clinical Oncology* 27:6144-6151.
 - 24) Duffy, MJ, Napieralski R, Martens JW, Span PN, Spyrtatos F, Sweep FC, Brunner N, Foekens JA, **Schmitt M**. EORTC PathoBiology Group. (2009). Methylated genes as new cancer biomarkers. *European Journal of Cancer* 45:335-346.
 - 25) Hartmann O, Spyrtatos F, Harbeck N, Dietrich D, Fassbender A, **Schmitt M**, Eppenberger-Castori S, Vuaroqueaux V, Lerebours F, Welzel K, Maier S, Plum A, Niemann S, Foekens JA, Lesche R, Martens JWM. (2009). DNA methylation markers predict outcome in node-positive, estrogen receptor-positive breast cancer with adjuvant anthracycline-based chemotherapy. *Clinical Cancer Research* 15:315-328.
 - 26) Specht K, Harbeck N, Smida J, Annecke K, Reich U, Naehrig J, Langer R, Mages J, Busch R, Kruse E, Klein-Hitpass L, **Schmitt M**, Kiechle M, Hoefler H. (2009). Expression profiling identifies genes that predict recurrence of breast cancer after adjuvant CMF-based chemotherapy. *Breast Cancer Research and*

- Treatment 118:45-56.
- 27) Zhang Y, Sieuwerts AM, McGreevy M, Casey G, Cufer T, Paradiso A, Harbeck N, Span PN, Hicks DG, Crowe J, Tubbs RR, Budd GT, Lyons J, Sweep FC, **Schmitt M**, Schittulli F, Golouh R, Talantov D, Wang Y, Foekens JA. (2009). The 76-gene signature defines high-risk patients that benefit from adjuvant tamoxifen therapy. *Breast Cancer Research and Treatment* 116:303-309.
 - 28) Debela M, Beaufort N, Magdolen V, Schechter NM, Craik CS, **Schmitt M**, Bode W, Goettig P. (2008). Structures and specificity of the human kallikrein-related peptidases KLK 4, 5, 6, and 7. *Biological Chemistry* 389:623-632.
 - 29) Sturgeon CM, Hoffman BR, Chan DW, Ch'ng SL, Hammond E, Hayes DF, Liotta LA, Petricoin EF, **Schmitt M**, Semmes OJ, Söletormos G, van der Merwe E, Diamandis EP; National Academy of Clinical Biochemistry. (2008). National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines for use of tumor markers in clinical practice: quality requirements. *Clinical Chemistry* 54:e1-e10.
 - 30) Harbeck N, Nimmrich I, Hartmann A, Ross JS, Cufer T, Grützmann R, Kristiansen G, Paradiso A, Hartmann O, Margossian A, Martens J, Schwöpe I, Kluth A, Müller V, Milde-Langosch K, Nährig J, Foekens J, Maier S, **Schmitt M**, Lesche R; on behalf of the EpiBreast Group. (2008). Multicenter study using paraffin-embedded tumor tissue confirms PITX2 DNA methylation as a marker for outcome prediction in tamoxifen-treated, node-negative breast cancer patients. *Journal of Clinical Oncology* 26:5036-5042.
 - 31) Dorn J, **Schmitt M**, Kates R, Schmalfeldt B, Kiechle M, Scorilas A, Diamandis EP, Harbeck N. (2007). Primary tumor levels of human tissue kallikreins affect surgical success and survival in ovarian cancer patients. *Clinical Cancer Research* 13:1742-1748.
 - 32) Maier S, Nimmrich I, Koenig T, Eppenberger-Castori S, Bohlmann I, Paradiso A, Spyrtatos F, Thomssen C, Mueller V, Nährig J, Schittulli F, Kates R, Lesche R, Schwöpe I, Kluth A, Marx A, Martens JW, Foekens JA, **Schmitt M**, Harbeck N; European Organisation for Research and Treatment of Cancer (EORTC) PathoBiology group. (2007). DNA-methylation of the homeodomain transcription factor PITX2 reliably predicts risk of distant disease recurrence in tamoxifen-treated, node-negative breast cancer patients--Technical and clinical validation in a multi-centre setting in collaboration with the European Organisation for Research and Treatment of Cancer (EORTC) PathoBiology group. *European Journal of Cancer* 43:1679-1686.
 - 33) Foekens JA, Atkins D, Zhang Y, Sweep FC, Harbeck N, Paradiso A, Cufer T, Sieuwerts AM, Talantov D, Span PN, Tjan-Heijnen VC, Zito AF, Specht K, Hoefler H, Golouh R, Schittulli F, **Schmitt M**, Beex LV, Klijn JG, Wang Y. (2006). Multicenter validation of a gene expression-based prognostic signature in lymph node-negative primary breast cancer. *Journal of Clinical Oncology* 24:1665-1671.
 - 34) Borgono CA, Kishi T, Scorilas A, Harbeck N, Dorn J, Schmalfeldt B, **Schmitt M**, Diamandis EP. (2006). Human kallikrein 8 protein is a favorable prognostic marker in ovarian cancer. *Clinical Cancer Research*. 12:1487-1493.
 - 35) Martens JW, Nimmrich I, Koenig T, Look MP, Harbeck N, Model F, Kluth A, Bolt-de Vries J, Sieuwerts AM, Portengen H, Meijer-Van Gelder ME, Piepenbrock C, Olek A, Hoefler H, Kiechle M, Klijn JG, **Schmitt M**, Maier S, Foekens JA. (2005). Association of DNA methylation of phosphoserine aminotransferase with response to endocrine therapy in patients with recurrent breast cancer. *Cancer Research* 65:4101-4117.
 - 36) Meijer-van Gelder ME, Look MP, Peters HA, **Schmitt M**, Brunner N, Harbeck N, Klijn JG, Foekens JA. (2004). Urokinase-type plasminogen activator system in breast cancer: association with tamoxifen therapy in recurrent disease. *Cancer Research* 64:4563-4568.
 - 37) Scorilas A, Borgono CA, Harbeck N, Dorn J, Schmalfeldt B, **Schmitt M**, Diamandis EP. Human kallikrein 13 protein in ovarian cancer cytosols: a new favorable prognostic marker. *Journal of Clinical Oncology* (2004); 22:678-685.
 - 38) Look M, van Putten W, Duffy M, **Schmitt M**, Foekens J. (2003). Pooled analysis of prognostic impact of uPA and PAI-1 in breast cancer patients. *Thrombosis and Haemostasis* 90:538-548.
 - 39) Yousef GM, Polymeris ME, Grass L, Soosaipillai A, Chan PC, Scorilas A, Borgono C, Harbeck N, Schmalfeldt B, Dorn J, **Schmitt M**, Diamandis EP. (2003). Human kallikrein 5: a potential novel serum biomarker for breast and ovarian cancer. *Cancer Research* 63:3958-3965.
 - 40) Kishi T, Grass L, Soosaipillai A, Scorilas A, Harbeck N, Schmalfeldt B, Dorn J, Mysliwiec M, **Schmitt M**, Diamandis EP. (2003). Human kallikrein 8, a novel biomarker for ovarian carcinoma. *Cancer Research* 63:2771-2774.
 - 41) Harbeck N, Kates RE, Look MP, Meijer-Van Gelder ME, Klijn JG, Kruger A, Kiechle M, Janicke F, **Schmitt M**, Foekens JA. (2002). Enhanced benefit from adjuvant chemotherapy in breast cancer patients classified high-risk according to urokinase-type plasminogen activator (uPA) and plasminogen activator inhibitor type 1 (n = 3424). *Cancer Research* 62:4617-4622.
 - 42) Look MP, van Putten WL, Duffy MJ, **Schmitt M**, Foekens JA. (2002). Pooled analysis of prognostic impact of urokinase-type plasminogen activator and its inhibitor PAI-1 in 8377 breast cancer patients. *Journal of the National Cancer Institute* 94:116-128.
 - 43) Jänicke F, Prechtl A, Thomssen C, Harbeck N, Meisner C, Untch M, Sweep CG, Selbmann HK, Graeff H, **Schmitt M**; German N0 Study Group. (2001). Randomized adjuvant chemotherapy trial in high-risk, lymph node-negative breast cancer patients identified by urokinase-type plasminogen activator and plasminogen activator inhibitor type 1. *Journal of the National Cancer Institute* 93:913-920.