CV

SCIENTIFIC CAREER

since 10.2021 — Integration of the research group into the National Center of Tumor Diseases (NCT), Technical University of Dresden

08.2012 – 10.2021 — Integration of the research group into the Center of Regenerative Therapies Dresden (CRTD), Technical University of Dresden

since 01.04.2012 — Research group leader of „Experimental Dermatology“, Department of Dermatology, University Hospital Carl Gustav Carus, Technical University of Dresden

- *Main research topics:*
  - *Establishing 3-dimensional full-skin melanoma-spheroid models as pre-clinical screening systems*
  - *Analyzing the influence of the tumor microenvironment on the therapeutic outcome of melanoma metastases*
  - *Identifying sensitive nodes in the signal transduction network of melanoma as therapeutic targets*
  - *Validating/Development of predictive Systems Biological models regarding resistance of malignant melanoma against combination therapy*
  - *Investigating the molecular cross talk between the antagonizing transcription factors NFκB and p53 in the development of squamous cell carcinoma (SCC)*
  - *Investigating a novel nuclear function of caspase-8 in cancer progression*

08.2004 - 03.2012 — Assistant Professor and Group Leader of „Molecular and Cellular Biology“ at the Institute of Cell Biology and Immunology at the University of Stuttgart

- *Main research topics:*
  - *Changes in the physiological output of NFκB: turning from an anti- into a pro-apoptotic factor*
  - *Modelling and analysis of the NFκB-dependent enhancement of UVB-induced apoptosis*

- *Investigating the interplay of chemotherapeutic drugs, p53 and NFκB in SCC therapy*
- *Dissecting the tumor selectivity of the death ligand TRAIL depending on the tumor progression stage of malignant melanoma*

02.1997 - 07.2004	Postdoc and PI at the Laboratory of Cell Biology at the Department of Dermatology of the Westfälische-Wilhelms University of Münster
17.06.2003	Habilitation in: „Molecular and Cellular Biology“

- *Main research topic: Molecular mechanisms of UV-induced signal transduction and apoptosis*

10.1993 – 12.1996	PhD student at the Institute of Biochemistry at the Medical University of Lübeck

- *Main research topic: Characterizing thermostable RNases from extremophile Archaea*

AWARDS

2021	Oscar-Gans Research Award in Experimental Dermatology
2009	German Skin Cancer Award (in collaboration with Prof. Meier, Tübingen)
2000	Graduate Award of the Novartis-Foundation for therapeutic research in the fields of Haemostaseology und Oncology
1999	Albert Kligman Fellowship of the Society of Investigative Dermatology
1999	NIH Grant Award of Keystone Symposia

PEER REVIEWED ORIGINAL PAPERS (10 years)

1. Del Mistro G, Riemann S, Schindler S, Beissert S, Kontermann RE, Ginolhac A, Helder R, Presta L, Sinkkonen L, Sauter T, **Kulms D**: Focal adhesion kinase plays a dual role in TRAIL resistance and metastatic outgrowth of malignant melanoma. **Cell Death Dis**, in press (2021)

2. Montinaro A, Zubiaur IA, Saggau J, Kretz A-L, Ferreira RMM, Hassan O, Kitzig E, Mueller I, El-Bahrawy M, von Karstedt S, **Kulms D**, Liccardi G, Lemke J, Walczak H: Potent pro-apoptotic combination therapy is highly effective in a broad range of cancers. **Cell Death Differ,** doi: 10.1038/s41418-021-00869-x (2021)

3. Phan TS, Schink L, Mann J, Merk VM, Zwicky P, Mundt S, Simon D, **Kulms D**, Albrecht S, Legler DF, Noti M, Brunner T: Keratinocytes control skin immune homeostasis through de novo-synthesized glucocorticoids. **Sci Advances,** 7(5):eabe0337. doi: 10.1126/sciadv.abe0337. (2021)

4. Vetma V, Guttà C, Peters N, Praetorius C, Hutt M, Seifert O, Meier F, Kontermann R, **Kulms D**, Rehm M: Convergence of pathway analysis and pattern recognition predicts sensitization to latest generation TRAIL therapeutics by IAP antagonism. **Cell Death Differ**, doi: 10.1038/s41418-020-0512-5. (2020)

5. Müller I, Strozyk E, Schindler S, Beissert S, Zarni Oo H, Sauter T, Lucarelli P, Raeth S, Hausser A, Al Nakouzi N, Fazli L, Gleave M, Liu H, Simon HU, Walczak H, Green DR, Bartek J, Daugaard M, **Kulms D:** Cancer cells employ nuclear caspase-8 to promote tumor progression by overcoming the p53-dependent G2/M checkpoint through cleavage of the de-ubiquitinase USP28. **Mol Cell**, doi: 10.1016/j.molcel.2019.12.023. (2020)

6. Pacheco MP, Bintener T, Ternes D, **Kulms D**, Haan S, Letellier E, Sauter T. Identifying and targeting cancer-specific metabolism with network-based drug target prediction. **EBioMedicine**. 43:98-106. doi: 10.1016/j.ebiom.2019.04.046. (2019)

7. Margue C, Philippidou D, Kozar I, Cesi G, Felten P, **Kulms D**, Letellier E, Haan C, Kreis S: Kinase inhibitor library screening identifies synergistic drug combinations effective in sensitive and resistant melanoma cells. **J Exp Clin Cancer Res,** 38:56. doi: 10.1186/s13046-019-1038-x (2019)

8. Del Mistro G, Lucarelli P, Müller I, De Landtsheer S, Zinoveva A, Hutt M, Siegemund M, Kontermann RE, Beissert S, Sauter T, **Kulms D**: Systemic network analysis identifies XIAP and IκBα as potential drug targets in TRAIL resistant BRAF mutated melanoma. **NPJ Syst Biol Appl** 4:39; doi: 10.1038/s41540-018-0075-y (2018)

9. Rožanc J, Sakellaropoulos T, Antoranz A, Guttà C, Podder B, Vetma V, Pliaka V, Sauter T, **Kulms D**, Rehm M, Alexopoulos LG: Phosphoprotein patterns allow predicting of trametinib responsiveness and optimal trametinib sensitization strategies in melanoma. **Cell Death Differ**, doi: 10.1038/s41418-018-0210-8 (2018)

10. Müller I, **Kulms D**: 3D organotypic melanoma-spheroid-skin-model. **J Vis Exp**, (135). doi: 10.3791/57500 (2018)

11. Siegemund M, Schneider F, Hutt M, Seifert O, Müller I, **Kulms D**, Pfizenmaier K, Kontermann RE: EGFR-targeted IgG-single-chain TRAIL fusion proteins for tumor therapy. **Scientific Reports**, doi: 10.1038/s41598-018-24450-8. (2018); **IF: 4,5**

12. Hutt M, Marquardt L, Seifert O, Siegemund M, Müller I, **Kulms D**, Pfizenmaier K, Kontermann RE: Superior properties of Fc-comprising scTRAIL fusion proteins. **Mol Cancer Ther,** pii: molcanther.0551.2017. doi: 10.1158/1535-7163.MCT-17-0551. (2017); **IF: 5,1**

13. Niessner H, Sinnberg T, Smalley KSM, Beck D, Praetorius, Mai M, Beissert S, **Kulms D**, Schaller M, Garbe C, Flaherty K, Westphal D, Wanke I, Meier F: BRAF inhibitors amplify the pro-apoptotic activity of MEK inhibitors by inducing ER stress in NRAS-mutant melnaoma. **Clin Cancer Res,** 23:6203-6214. doi: 10.1158/1078-0432.CCR-17-0098. (2017)

14. Niessner H, Schmitz J, Tabatabai G, Schmid AM, Calaminus C, Sinnberg T, Weide B, Garbe C, Schittek B, Quintanilla-Fend L, Mai M, Praetorius C, Beissert S, Schackert G, Muders M, Meinhardt M, Baretton G, Dummer R, Flaherty K, Pichler BJ, **Kulms D**, Westphal D, Meier F: PI3K pathway inhibition achieves potent antitumor activity in melanoma brain metastases *in vitro* and *in vivo*. **Clin Cancer Res,** 10.1158/1078-0432.CCR-16-0064. (2016)

15. Heulot M, Chevalier N, Puyal J, Margue C, Michel S, Kreis S, **Kulms D**, Nahimana A, Widmann C: The TAT-RasGAP317-326 anti-cancer peptide activates apoptosis and an uncharacterized alternate mode of death. **Oncotarget**, 7(39):64342-64359. doi: 10.18632/oncotarget.11841. (2016)

16. Henry CM, Sullivan GP, Clancy DM, Afonina IS, **Kulms D**, Martin SJ: Neutrophil-derived Proteases Escalate Inflammation through Activation of IL-36 family cytokines. **Cell Rep**, 14: 708-722. doi: 10.1016/j.celrep.2015.12.072. (2016)

17. Müller I, Beissert S, **Kulms D**: Anti-apoptotic NFκB and "gain of function" *mut*p53 in concert act pro-apoptotic in response to UVB+IL-1 *via* enhanced TNF production. **J Invest Dermatol**, doi: 10.1038/jid.2014.481. (2015)

18. Bullenkamp J, Raulf N, Ayaz B, Walczak H, **Kulms D**, Thavaraj S, Odell E, Tavassoli M: Bortezomib sensitises TRAIL-resistant HPV positive head and neck cancer cells to TRAIL through a caspase-dependent, E6-independent mechanism. **Cell Death Dis**, 5:e1489. doi: 10.1038/cddis.2014.455. (2014)

19. Raulf N, El-Attar R, **Kulms D**, Lecis D, Delia D, Walczak H, Papenfuss K, Odell E, Tavassoli M: Differential response of head and neck cancer cell lines to TRAIL or Smac mimetics is associated with the cellular levels and activity of caspase-8 and caspase-10. **Br J Cancer**, 111:1955-64. doi: 10.1038/bjc.2014.521. (2014)

20. Konrath F, Witt J, Sauter T, **Kulms D**: Identification of new IκBα complexes by an iterative experimental and mathematical modeling approach. **PLoS Comp Biol** doi: 10.1371/journal.pcbi.1003528 (2014)

21. Vörsmann H, Gröber F, Walles H, Beissert S, Walczak H**, Kulms D**: Development of a human three-dimensional organotypic skin-melanoma spheroid model for in vitro drug testing. **Cell Death Dis** doi: 10.1038/cddis.2013.249. (2013)

22. Niessner H, Forschner A, Klumpp B, Honegger JB, Witte M, Bornemann A, Dummer R, Adam A, Bauer J, Tabatabai G, Flaherty K, Sinnberg T, Beck D, Leiter U, Mauch C, Roesch A, Weide B, Eigentler T, Schadendorf D, Garbe C, **Kulms D**, Quintanilla-Martinez L, Meier F: Targeting hyperactivation of the AKT survival pathway to overcome therapy resistance of melanoma brain metastases. **Cancer Med** doi: 10.1002/cam4.50. (2013)

23. Beck D, Niessner H, Smalley KS, Flaherty K, Paraiso KH, Busch C, Sinnberg T, Vasseur S, Iovanna JL, Drießen S, Stork B, Wesselborg S, Schaller M, Biedermann T, Bauer J, Lasithiotakis K, Weide B, Eberle J, Schittek B, Schadendorf D, Garbe C, **Kulms D**, Meier F: Vemurafenib potently induces endoplasmic reticulum stress-mediated apoptosis in BRAFV600E melanoma cells. **Sci Signal** 6(260):ra7. doi: 10.1126/ scisignal.2003057. (2013)

24. Witt, JF, Konrath F, Sawodny O, Ederer M, **Kulms D**, Sauter T: Analysing the role of UVB-induced translational inhibition and PP2Ac deactivation in NF-κB signalling using a minimal mathematical model. **PLoS One ,** 7:e40274 (2012)

25. Witt J, Barisic S, Sawodny O, Ederer M, **Kulms D**, Sauter T: Modelling time delay in the NFkappaB signaling pathway following low dose IL-1 stimulation. **EURASIP J Bioinform Syst Biol** 3: 1-6 (2011)

26. Niessner H, Sinnberg T, Beck D, Lasithiotakis K, Maczey E, Venturelli S, Berger A, Mauthe M, Toulany M, Flaherty K, Schaller M, Schadendorf D, Proikas-Cezanne T, Schittek B, Garbe C, **Kulms D,** Meier F: The farnesyl transferase inhibitor lonafarnib inhibits mTOR signalling and enforces sorafenib-induced apoptosis in melanoma cells. **J Invest Dermatol** 131: 468-479 (2011)

27. Hörnle M, Peters N, Thayaparasingham B, Vörsmann H, Kashkar H, **Kulms D**: Caspase-3 cleaves XIAP in a positive feedback loop to sensitize melanoma cells to TRAIL-induced apoptosis. **Oncogene** 30: 575-587 (2010)

28. Barisic S, Schmidt C, Walczak H, **Kulms D**: Tyrosine phosphatase inhibition triggers sustained canonical Serine-dependent NFκB activation via Src-dependent blockade of PP2A. **Biochem Pharmacol** 80: 439-447 (2010)

29. Witt J, Barisic S, Schumann E, Allgöwer F, Sawodny O, Sauter T, **Kulms D**: Mechanism of PP2A-mediated IKKβ dephosphorylation: a systems biological approach. **BMC Syst Biol** 3: 71 (2009)

30. Sinnberg T, Lasithiotakis K, Niessner H, Schittek B, Flaherty K, **Kulms D**, Maczey E, Campos M, Gogel J, Garbe C, Meier F: Inhibition of PI3K-AKT-mTOR signalling

sensitizes melanoma cells to cisplatin and temozolomide. **J Invest Dermatol** 129: 1500-1515 (2009)

31. Thayaparasingham B, Kunz A, **Kulms D**: Sensitization of Melanoma Cells to TRAIL by UVB-induced and NFκB-mediated Downregulation of xIAP. **Oncogene** 28: 345-362 (2009)

32. Barisic S, Strozyk E, Peters N, Walczak H, **Kulms D**: Identification of PP2A as a crucial regulator of the NF-kappaB feedback loop: its inhibition turns NF-kappaB into a pro-apoptotic factor. **Cell Death Differ** 15: 1681-1690 (2008)

33. Lasithiotakis KG, Sinnberg TW, Schittek B, Flaherty KT, **Kulms D**, Maczey E, Garbe C, Meier F: Combined Inhibition of MAPK and mTOR signalling inhibits growth, induces cell death, and abrogates invasive growth of melanoma cells. **J Invest Dermatol**, 128: 2013-2023 (2008)

34. Witt J, Husser S, **Kulms D**, Barisic S, Sawodny O, Sauter T: Modeling of IL-1 induced NF-kappaB signaling and analysis of additional UVB influence. **SICE Annu Conf** 1353-1358 (2007)

35. Meier F, Busch S, Lasithiotakis K, **Kulms D**, Garbe C, Maczey E, Herlyn M, Schittek B: Combined targeting of MAPK and AKT signalling pathways is a promising strategy for melanoma treatment. **Br J Dermatol** 156: 1204-1213 (2007)

36. Strozyk E, Pöppelmann B, Schwarz T, **Kulms D**: Differential effects of NFκB on apoptosis induced by DNA-damaging agents: The type of DNA damage determines the final outcome. **Oncogene**, 25: 6239-6251 (2006)

37. Pöppelmann B, Klimmek K, Strozyk E, Voss R, Schwarz T, **Kulms D**: NFκB- dependent downregulation of TRAF proteins contributes to IL-1 mediated enhancement of UVB-induced apoptosis. **J Biol Chem** 280: 15635-15643 (2005)

38. Zeise E, Weichenthal M, Schwarz T, **Kulms D**: Resistance of human melanoma cells against the death ligand TRAIL is reversed by ultraviolet-B radiation. **J Invest Dermatol** 123: 746-754 (2004)

39. **Kulms D**, Zeise E, Pöppelmann B, Schwarz T: DNA damage, death receptor activation and reactive oxygen species contribute to ultraviolet radiation-induced apoptosis in an essential and independent way. **Oncogene** 21: 5844-5851 (2002)

40. **Kulms D,** Düßmann H, Pöppelmann B, Ständer S, Schwarz A, Schwarz T: Apoptosis induced by disruption of the cytoskeleton is mediated via activation of CD95 (Fas/APO-1). **Cell Death Diff** 9: 598-608 (2002)

41. Schwarz A, Ständer S, Berneburg M, Böhm M, **Kulms D**, van Steeg H, Große-Heitmeyer K, Krutmann J, Schwarz T: Interleukin-12 suppresses ultraviolet radiation-induced apoptosis by inducing DNA repair. **Nat Cell Biol** 4: 26-31 (2002)

42. **Kulms D,** Schwarz T: Ultraviolet radiation inhibits interleukin-2-induced tyrosine phosphorylation and the activation of STAT5 in T lymphocytes. **J Biol Chem** 276: 12849-12855 (2001)

43. **Kulms D,** Pöppelmann B, Schwarz T: Ultraviolet radation-induced interleukin 6 release in HeLa cells is mediated via membrame events in a DNA damage-independent way. **J Biol Chem** 275: 15060-15066 (2000)

44. **Kulms D,** Pöppelmann B, Yarosh D, Luger T, Krutmann J, Schwarz T: Nuclear and cell membrane effects contribute independently to the induction of apoptosis in human cells exposed to UVB radiation. **Proc Natl Acad Sci USA** 96: 7974-7979 (1999)

45. Kothny-Wilkes G, **Kulms D,** Luger TA, Kubin M, Schwarz T: Interleukin-1 protects transformed keratinocytes from tumor necrosis factor-related apoptosis-inducing ligand- and CD95-induced apoptosis but not from ultraviolet radiation-induced apoptosis. **J Biol Chem** 274: 28916-28921 (1999)

46. Aragane Y, **Kulms D,** Metze D, Kothny G, Pöppelmann B, Luger TA, Schwarz T: Ultraviolet light induces apoptosis via direct activation of CD95 (FAS/APO-1) independently from its ligand CD95L. **J Cell Biol** 140: 171-182 (1998)

47. Kothny-Wilkes G, **Kulms D,** Pöppelmann B, Luger TA, Kubin M, Schwarz T: Interleukin-1 protects transformed keratinocytes from TRAIL- induced apoptosis. **J Biol Chem** 273: 29247-29253 (1998)

48. Aragane Y, **Kulms D,** Luger TA, Schwarz T: Downregulation of interferon γ-activated STAT1 by UV light. **Proc Natl Acad Sci USA** 94: 11490-11495 (1997)

49. **Kulms D,** Schäfer G, Hahn U: Overproduction of Sac7d and Sac7e reveals only Sac7e to be a DNA-binding protein with ribonuclease activity from the extremophilic archaeon *Sulfolobus acidocaldarius*. **Biol Chem** 378: 545-551 (1997)

50. **Kulms D,** Schäfer G, Hahn U: SARD, a new protein isolated from the extremophile archaeon *Sulfolobus acidocaldarius*, is a thermostable ribonuclease with DNA-binding properties. **Biochem Biophys Res Comm** 214: 646-652 (1995)

INVITED BOOK CHAPTERS

1. **Kulms D**, Meier F: *In vitro* models of melanoma. In: **Skin Tissue Models**, Eds.: AP Marques, RP Pirraco, MT Cerqueria, RL Reis; Elsevier Inc, Camebridge; ISBN: 978-0-12-810545-0 (2018)

2. Schwarz T, **Kulms D**: NFκB and cytokines. In: **Vitamins and Hormones**, Vol. 74: Interleukins. Ed.: G. Litwack, Acadmic Press, San Diego, 284-296 (2006)

3. **Kulms D**, Schwarz T: Ultraviolet radiation and apoptosis. In: **UV-induced melanogenesis**. Eds.: J-P. Ortonne, Martin Dunitz Ltd., London, 262-266 (2002)

INVITED REVIEWS

1. Albrecht M, Lucarelli P, **Kulms D**, Sauter T: Computational models of melanoma. **Theor Biol Med Model**. 17:8. doi: 10.1186/s12976-020-00126-7 (2020)

2. Linkermann A, **Kulms D**: Cell death and regeneration in Dresden-the 27th meeting of the European Cell Death Organization. **Cell Death Dis** 10:910. doi: 10.1038/s41419-019-2153-5 (2020)

3. Busch S, **Kulms D**: Organotypische 3D-Zellkultur-Modelle: Dreidimensionale Vollhaut-rekonstrukte als Modelle humaner Erkrankungen. **Biospektrum** 04/15: 392-394. doi: 10.1007/s12268-015-0592-9 © Springer-Verlag (2015)

4. Strozyk E, **Kulms D**: The role of AKT/mTOR pathway in stress response to UV-irradiation: implication in skin carcinogenesis by regulation of apoptosis, autophagy and senescence. **Int J Mol Sci** 14:15260-15285. doi: 10.3390/ijms140815260 (2013)

5. Strozyk E, Wysocki JP, **Kulms D**: Combination therapy of skin cancer: Cytokines and apoptosis. **Clin Derm: Retinoids & other Treatments.** 8: 1-6 (2006)

6. Strozyk E, **Kulms D**: NFκB: Cell survival or cell death? **Signal Transduction** 5: 334-349 (2005).

7. **Kulms D**, Schwarz T: 20 years after – Milestones in molecular photobiology. **J Invest Dermatol Symp Proc**, 7(1): 46-50 (2002)

8. **Kulms D**, Schwarz T: Molecular mechanisms involved in UV induced apoptotic cell death. **Skin Pharmacol Appl Skin Physiol** 15: 342-347 (2002)

9. **Kulms D**, Schwarz T: Independent contribution of three different pathways to ultraviolet-B-induced apoptosis. **Biochem Pharmacol** 64: 837-841 (2002)

10. **Kulms D**, Schwarz T: UV-induced signal transduction pathways. **J Dermatol** 29: 189-196 (2002)
11. Murphy G, Young AR, Wulf HC, **Kulms D,** Schwarz T: The molecular determinants of sunburn cell formation. **Exp Dermatol** 10: 195-201 (2001)
12. **Kulms D**, Schwarz T: Molecular mechanisms of UV-induced apoptosis. **Photodermatol Photoimmunol Photomed** 16: 195-201 (2000)