

Curriculum vitae



1) Biographical details

Surname, name: von Felden, Johann
Academic title: Dr. med. (MD)
Date of birth: September 30th, 1985
Business adress: 1. Medizinische Klinik und Poliklinik, Universitätsklinikum Hamburg-Eppendorf, Martinistr. 52, 20246 Hamburg, 040 / 7410-53910
E-Mail: j.von-felden@uke.de
Current Position: Facharzt Innere Medizin (Resident for Internal Medicine), Wissenschaftlicher Mitarbeiter

2) Education / Training

2006 – 2012 Medical School Hannover
2013 Doctoral thesis defense Dr. med. (M.D.) Internal Medicine / Cardiology, Medical School Hannover, magna cum laude. Supervisor: PD Dr. Udo Bavendiek

3) Professional experience

Since 05/2013: 1. Dept. of Internal Medicine, University Medical Center Hamburg Eppendorf (UKE), Directors: Prof. Ansgar W. Lohse and Prof. Samuel M. Huber
Since 2015: Deputy-PI and Sub-Investigator on several clinical trials in liver cancer
06/2017 – 05/2019: Postdoctoral Fellowship (DFG-funded), Tisch Cancer Institute, Mount Sinai Hospital New York, USA. Supervisor: Prof. Augusto Villanueva, Program Directors: Prof. Josep M. Llovet and Prof. Scott Friedman
11/2021 Board certification for Internal Medicine (Facharzt Innere Medizin)

4) Honors and Awards

Young Investigator Bursary der EASL, International Liver Congress 2016
Young Investigator Bursary der EASL, HCC Summit 2017
Poster of Distinction, AASLD Liver Meeting 2019
Top Scored Poster, Annual Meeting International Liver Cancer Association (ILCA) 2019
Young Investigator Bursary der EASL, International Liver Congress 2020
Young Investigator Bursary der EASL, HCC Summit 2020

5) Memberships

Deutsche Gesellschaft für Gastroenterologie, Verdauungs- und Stoffwechselkrankheiten (DGVS)
European Association for the Study of the Liver (EASL)
American Association for the Study of Liver Diseases (AASLD)
American Association for Cancer Research (AACR)
International Liver Cancer Association (ILCA)

6) Patents issued

Application Title: Small, unannotated, non-coding, RNAs for the Detection of Liver Cancer. Serial Number: 62/938,493 (United States Patent Office)

7) Secured Funding

2017-2019 DFG Research Fellowship, ca. 100.000 Euro (FE1746/1-1)
2019-2022 Clinician Scientist Program University Medical Center Hamburg Eppendorf, 50% Clinical Leave for 3 years

2020/2021	Internal Funding University Medical Center Hamburg Eppendorf, 26.000 EUR
2021	Freistellungs-Stipendium (clinical leave), Deutsche Leberstiftung, ca. 20.000 EUR
2021	DFG Research grant, 3 years, ca. 350.000 Euro (FE1746/3-1)
2022-2025	BMBF-funded Advanced Clinician Scientist Programm (iSTAR) UKE, ca. 1.000.000 Euro

8) Publications, total >50 articles, h-Index 21,

for full list please see <https://pubmed.ncbi.nlm.nih.gov/?term=von+felden&sort=date>

8.1. Five highlighted publications

Unannotated small RNA clusters in circulating extracellular vesicles detect early stage liver cancer.

von Felden, J., Garcia-Lezana, T., Dogra, N., Kozlova, E., Ahsen, M. E., Craig, A. J., Gifford, S., Wunsch, B., Smith, J. T., Kim, S., Diaz, J. E. L., Chen, X., Labgaa, I., Haber, P. K., Olsen, R., Han, D., Restrepo, P., D'Avola, D., Hernandez-Meza, G., Allette, K., Sebra, R., Saberi, B., Tabrizian, P., Asgharpour, A., Dieterich, D., Llovet, J. M., Cordon-Cardo, C., Tewari, A., Schwartz, M., Stolovitzky, G., **Losic, B., Villanueva, A.**, Published Online First: 28 July 2021 in : **GUT**. doi: 10.1136/gutjnl-2021-325036. (last impact factor **23.06**)

Mutations in circulating tumor DNA predict primary resistance to systemic therapies in advanced hepatocellular carcinoma

von Felden, J., Craig, A. J., Garcia-Lezana, T., Labgaa, I., Haber, P. K., D'Avola, D., Asgharpour, A., Dieterich, D., Bonaccorso, A., Torres-Martin, M., Sia, D., Sung, M. W., Tabrizian, P., Schwartz, M., Llovet, J. M. & Villanueva, A., 01.2021, in : **ONCOGENE**. 40, 1, S. 140-151 12 S. (last impact factor **9.87**)

Tumour evolution in hepatocellular carcinoma

Craig, A. J., **von Felden, J.**, Garcia-Lezana, T., Sarcognato, S. & Villanueva, A., 03.2020, in : **NAT REV GASTRO HEPAT**. 17, 3, S. 139-152 14 S. (last impact factor **46.80**)

β -Catenin Activation Promotes Immune Escape and Resistance to Anti-PD-1 Therapy in Hepatocellular Carcinoma

Ruiz de Galarreta, M., Bresnahan, E., Molina-Sánchez, P., Lindblad, K. E., Maier, B., Sia, D., Puigvehi, M., Miguela, V., Casanova-Acebes, M., Dhainaut, M., Villacorta-Martin, C., Singhi, A. D., Moghe, A., **von Felden, J.**, Tal Grinspan, L., Wang, S., Kamphorst, A. O., Monga, S. P., Brown, B. D., Villanueva, A., Llovet, J. M., Merad, M. & Lujambio, A., 08.2019, in : **CANCER DISCOV**. 9, 8, S. 1124-1141 18 S. (last impact factor **39.4**)

Intratumoral heterogeneity and clonal evolution in liver cancer

Losic, B., Craig, A. J., Villacorta-Martin, C., Martins-Filho, S. N., Akers, N., Chen, X., Ahsen, M. E., **von Felden, J.**, Labgaa, I., D'Avola, D., Allette, K., Lira, S. A., Furtado, G. C., Garcia-Lezana, T., Restrepo, P., Stueck, A., Ward, S. C., Fiel, M. I., Hiotis, S. P., Gunasekaran, G., Sia, D., Schadt, E. E., Sebra, R., Schwartz, M., Llovet, J. M., Thung, S., Stolovitzky, G. & Villanueva, A., 15.01.2020, in : **NAT COMMUN**. 11, 1, S. 291 (last impact factor **14.92**)

8.2. Other publications (last five years)

8.2.1. First author

- **Experimental Models of Liquid Biopsy in Hepatocellular Carcinoma Reveal Clone-Dependent Release of Circulating Tumor DNA**
Labgaa, I., **von Felden, J.***, Craig, A. J., Martins-Filho, S. N., Villacorta-Martin, C., Demartines, N., Dormond, O., D'Avola, D. & Villanueva, A., 06.2021, in : **HEPATOL COMM**. 5, 6, S. 1095-1105 11 S. (last impact factor **5.07**) *shared first authors
- **DNA methylation profiling of human hepatocarcinogenesis**

Hernandez-Meza, G., **von Felden, J.***, Gonzalez-Kozlova, E. E., Garcia-Lezana, T., Peix, J., Portela, A., Craig, A. J., Sayols, S., Schwartz, M., Losic, B., Mazzaferro, V., Esteller, M., Llovet, J. M. & Villanueva, A., 25.11.2020, in : **HEPATOLOGY**. (last impact factor 17.43) **shared first authors*

- **Sequential Systemic Treatment in Advanced Hepatocellular Carcinoma Is Able to Prolong Median Survival to More than 3 Years in a Selected Real-World Cohort.**
von Felden J, Karkmann K, Ittrich H, Gil-Ibanez I, Fründt T, Krause J, Lohse AW, Wege H, Schulze K. in: **VISC MED**. 2021 Mar;37(2):87-93. (last impact factor NA)
- **Elevated Aspartate Aminotransferase to Alanine Aminotransferase Ratio Predicts Poor Outcome in Hepatocellular Carcinoma**
von Felden, J., Wege, H. & Schulze, K., 09.2020, in : **HEPATOL COMM**. 4, 9, S. 1382-1383 2 S. (last impact factor 5.07)
- **The burden of hepatitis E among patients with haematological malignancies: A retrospective European cohort study**
von Felden, J., Alric, L., Pischke, S., Aitken, C., Schlabe, S., Spengler, U., Giordani, M. T., Schnitzler, P., Bettinger, D., Thimme, R., Xhaard, A., Binder, M., Ayuk, F., Lohse, A. W., Cornelissen, J. J., de Man, R. A. & Mallet, V., 09.2019, in : **J HEPATOL**. 71, 3, S. 465-472 8 S. (last impact factor 25.08)
- **High efficacy of sofosbuvir/velpatasvir and impact of baseline resistance-associated substitutions in hepatitis C genotype 3 infection**
von Felden, J.*, Vermehren, J., Ingiliz, P., Mauss, S., Lutz, T., Simon, K. G., Busch, H. W., Baumgarten, A., Schewe, K., Hueppe, D., Boesecke, C., Rockstroh, J. K., Daeumer, M., Luebke, N., Timm, J., Schulze Zur Wiesch, J., Sarrazin, C. & Christensen, S., 05.2018, in : **ALIMENT PHARM THER**. 47, 9, S. 1288-1295 8 S. (last impact factor 8.17) **shared first authors*
- **Circulating tumor cells as liquid biomarker for high HCC recurrence risk after curative liver resection**
von Felden, J.*, Schulze, K., Krech, T., Ewald, F., Nashan, B., Pantel, K., Lohse, A. W., Riethdorf, S. & Wege, H., 27.10.2017, in : **ONCOTARGET**. 8, 52, S. 89978-89987 10 S. (last impact factor 5.17) **shared first authors*
- **High expression of micro RNA-135A in hepatocellular carcinoma is associated with recurrence within 12 months after resection**
von Felden, J., Heim, D., Schulze, K., Krech, T., Ewald, F., Nashan, B., Lohse, A. W. & Wege, H., 18.01.2017, in : **BMC CANCER**. 17, 1, S. 60 (last impact factor 4.43)
- **Milde Covid-19-Verläufe bei Mitarbeitenden einer Universitätsklinik.**
von Felden J, Brehm TT, Schulze-zur-Wiesch J, Addo MM, Lohse AW, Knobloch J, Koch T, Published online 10.08.2021 in: **Bundesgesundheitsblatt**. <https://doi.org/10.1007/s00103-021-03396-9> (last impact factor 1.51)

8.2.2. Reviews

- **Liquid biopsy in the clinical management of hepatocellular carcinoma**
von Felden, J., Garcia-Lezana, T., Schulze, K., Losic, B. & Villanueva, A., 11.2020, in : **GUT**. 69, 11, S. 2025-2034 10 S. (last impact factor 23.06)
- **Role of Molecular Biomarkers in Liver Transplantation for Hepatocellular Carcinoma**
von Felden, J. & Villanueva, A., 06.2020, in : **LIVER TRANSPLANT**. 26, 6, S. 823-831 9 S. (last impact factor 5.80)
- **New systemic agents for hepatocellular carcinoma: an update 2020**
von Felden, J., 05.2020, in : **CURR OPIN GASTROEN**. 36, 3, S. 177-183 7 S. (last impact factor 3.29)
- **Rare variants of primary liver cancer: Fibrolamellar, combined, and sarcomatoid hepatocellular carcinomas.**
Wege H, Schulze K, **von Felden J**, Calderaro J, Reig M; rare liver tumors working group of the European Reference Network on Hepatological Diseases (ERN RARE-LIVER). 11.2021, in: **Eur J Med Genet**. 64(11):104313. doi: 10.1016/j.ejmg.2021.104313. Epub 2021 Aug 18.
- **The Impact of Translational Research in Hepatology**
von Felden, J., Craig, A. J. & Villanueva, A., 01.2019, in : **Clin Liver Dis (Hoboken)**. 13, 1, S. 29-33 5 S. (no impact factor yet)
- **Role of circulating tumor DNA to help decision-making in hepatocellular carcinoma**
von Felden, J., Craig, A. J. & Villanueva, A., 07.2018, in : **Oncoscience**. 5, 7-8, S. 209-211 3 S. (no impact factor yet)
- **Molecular profiling of liver cancer heterogeneity**
Craig, A. J., **von Felden, J.** & Villanueva, A., 09.2017, in : **DISCOV MED**. 24, 131, S. 117-125 9 S. (last impact factor 2.97)
- **First- and Second-Line Targeted Systemic Therapy in Hepatocellular Carcinoma-An Update on Patient Selection and Response Evaluation**

von Felden, J., Schulze, K., Gil-Ibanez, I., Werner, T. & Wege, H., 28.11.2016, in : **DIAGNOSTICS**. 6, 4, S. E44 (last impact factor 3.71)

8.2.3. Co-author

- **Prognosis of patients with hepatocellular carcinoma treated with immunotherapy - development and validation of the CRAFTY score.**
Scheiner B, Pomej K, Kirstein MM, Hucke F, Finkelmeier F, Waidmann O, Himmelsbach V, Schulze K, von Felden J, Fründt TW, Stadler M, Heinzl H, Shmanko K, Spahn S, Radu P, Siebenhüner AR, Mertens JC, Rahbari NN, Kütting F, Waldschmidt DT, Ebert MP, Teufel A, De Dosso S, Pinato DJ, Pressiani T, Meischl T, Balcar L, Müller C, Mandorfer M, Reiberger T, Trauner M, Personeni N, Rimassa L, Bitzer M, Trojan J, Weinmann A, Wege H, Dufour JF, Peck-Radosavljevic M, Vogel A, Pinter M. 11.10.2021, in: **J Hepatol**. ePub. doi:10.1016/j.jhep.2021.09.035. (last impact factor 25.08)
- **Early detection of hepatocellular carcinoma since the introduction of the German Clinical Practice Guideline in 2013.**
Schulze, K, von Felden, J, Fründt, TW, Krause, J, Werner, T, Casar, C, Jung, C, Ittrich, H, Sterneck, M, Li, J, Heumann, A, Fischer, L, Adam, G, Lohse, AW, Wege, H. 2021, in: **DTSCH ARZTEBL INT**. 118: 540-1 (last impact factor 5.59)
- **Transcriptomic characterization of cancer-testis antigens identifies MAGEA3 as a driver of tumor progression in hepatocellular carcinoma**
Craig, A. J., Garcia-Lezana, T., Ruiz de Galarreta, M., Villacorta-Martin, C., Kozlova, E. G., Martins-Filho, S. N., von Felden, J., Ahsen, M. E., Bresnahan, E., Hernandez-Meza, G., Labgaa, I., D'Avola, D., Schwartz, M., Llovet, J. M., Sia, D., Thung, S., Losic, B., Lujambio, A. & Villanueva, A., 06.2021, in : **PLOS GENET**. 17, 6, S. e1009589 (last impact factor 5.92)
- **Diagnostic and Prognostic Value of miR-16, miR-146a, miR-192 and miR-221 in Exosomes of Hepatocellular Carcinoma and Liver Cirrhosis Patients**
Fründt, T. W., Krause, L., Hussey, E., Steinbach, B., Köhler, D., von Felden, J., Schulze, K., Lohse, A. W., Wege, H. & Schwarzenbach, H., 19.05.2021, in : **CANCERS**. 13, 10 (last impact factor 6.64)
- **Hepatocellular carcinoma: Intratumoral EpCAM-positive cancer stem cell heterogeneity identifies high-risk tumor subtype**
Krause, J., von Felden, J., Casar, C., Fründt, T. W., Galaski, J., Schmidt, C., Jung, C., Ittrich, H., Weidemann, S. A., Krech, T., Heumann, A., Li, J., Fischer, L., Sauter, G., Lohse, A. W., Wege, H. & Schulze, K., 23.11.2020, in : **BMC CANCER**. 20, 1, S. 1130 (last impact factor 4.43)
- **Genetic variation in HSD17B13 reduces the risk of developing cirrhosis and hepatocellular carcinoma in alcohol misusers**
Stickel, F., Lutz, P., Buch, S., Nischalke, H. D., Silva, I., Rausch, V., Fischer, J., Weiss, K. H., Gotthardt, D., Rosendahl, J., Marot, A., Elamly, M., Krawczyk, M., Casper, M., Lammert, F., Buckley, T. W., McQuillin, A., Spengler, U., Eyer, F., Vogel, A., Marhenke, S., von Felden, J., Wege, H., Sharma, R., Atkinson, S., Franke, A., Nehring, S., Moser, V., Schafmayer, C., Spahr, L., Lackner, C., Stauber, R. E., Canbay, A., Link, A., Valenti, L., Grove, J. I., Aithal, G. P., Marquardt, J. U., Fateen, W., Zopf, S., Dufour, J-F., Trebicka, J., Datz, C., Deltre, P., Mueller, S., Berg, T., Hampe, J. & Morgan, M. Y., 07.2020, in : **HEPATOLOGY**. 72, 1, S. 88-102 15 S. (last impact factor 17.43)
- **GALAD Score Detects Early Hepatocellular Carcinoma in an International Cohort of Patients With Nonalcoholic Steatohepatitis**
Best, J., Bechmann, L. P., Sowa, J-P., Sydor, S., Dechêne, A., Pflanz, K., Bedreli, S., Schotten, C., Geier, A., Berg, T., Fischer, J., Vogel, A., Bantel, H., Weinmann, A., Schattenberg, J. M., Huber, Y., Wege, H., von Felden, J., Schulze, K., Bettinger, D., Thimme, R., Sinner, F., Schütte, K., Weiss, K. H., Toyoda, H., Yasuda, S., Kumada, T., Berhane, S., Wichert, M., Heider, D., Gerken, G., Johnson, P. & Canbay, A., 03.2020, in : **CLIN GASTROENTEROL H**. 18, 3, S. 728-735.e4 (last impact factor 11.38)
- **High rates of cirrhosis and severe clinical events in patients with HBV/HDV co-infection:longitudinal analysis of a German cohort:longitudinal analysis of a German cohort**
Bockmann, J-H., Grube, M., Hamed, V., von Felden, J., Landahl, J., Wehmeyer, M., Giersch, K., Hall, M. T., Murray, J. M., Dandri, M., Lüth, S., Lohse, A. W., Lütgehetmann, M. & Schulze Zur Wiesch, J., 30.01.2020, in : **BMC GASTROENTEROL**. 20, 1, S. 24 (last impact factor 3.07)
- **Treatment and re-treatment results of HCV patients in the DAA era**
Piecha, F., Gänßler, J-M., Ozga, A-K., Wehmeyer, M. H., Dietz, J., Kluwe, J., Laschtowitz, A., von Felden, J., Sterneck, M., Jordan, S., Pischke, S., Lohse, A. W. & Schulze Zur Wiesch, J., 2020, in : **PLOS ONE**. 15, 5, S. e0232773 (last impact factor 3.24)
- **Heterozygous carriage of the alpha1-antitrypsin Pi*Z variant increases the risk to develop liver cirrhosis**

- Strnad, P., Buch, S., Hamesch, K., Fischer, J., Rosendahl, J., Schmelz, R., Brueckner, S., Brosch, M., Heimes, C. V., Woditsch, V., Scholten, D., Nischalke, H. D., Janciauskiene, S., Mandorfer, M., Trauner, M., Way, M. J., McQuillin, A., Reichert, M. C., Krawczyk, M., Casper, M., Lammert, F., Braun, F., von Schönfels, W., Hinz, S., Burmeister, G., Hellerbrand, C., Teufel, A., Feldman, A., Schattenberg, J. M., Bantel, H., Pathil, A., Demir, M., Kluwe, J., Boettler, T., Ridinger, M., Wodarz, N., Soyka, M., Rietschel, M., Weber, T., Marhenke, S., Vogel, A., Hinrichsen, H., Canbay, A., Schlattjan, M., Sosnowsky, K., Sarrazin, C., **von Felden, J.**, Geier, A., Deltenre, P., Sipos, B., Schafmayer, C., Nothnagel, M., Aigner, E., Datz, C., Stickel, F., Morgan, M. Y., Hampe, J., Berg, T. & Trautwein, C., 06.2019, in : **GUT**. 68, 6, S. 1099-1107 9 S. (last impact factor 23.06)
- **Programmed cell death protein-1 (PD-1)-targeted immunotherapy in advanced hepatocellular carcinoma: efficacy and safety data from an international multicentre real-world cohort**
Scheiner, B., Kirstein, M. M., Hucke, F., Finkelmeier, F., Schulze, K., **von Felden, J.**, Koch, S., Schwabl, P., Hinrichs, J. B., Waneck, F., Waidmann, O., Reiberger, T., Müller, C., Sieghart, W., Trauner, M., Weinmann, A., Wege, H., Trojan, J., Peck-Radosavljevic, M., Vogel, A. & Pinter, M., 05.2019, in : **ALIMENT PHARM THER**. 49, 10, S. 1323-1333 11 S. (last impact factor 8.17)
 - **Chronic Hepatitis E in Rheumatology and Internal Medicine Patients: A Retrospective Multicenter European Cohort Study**
Pischke, S., Peron, J-M., von Wulffen, M., **von Felden, J.**, Höner Zu Siederdisen, C., Fournier, S., Lütgehetmann, M., Iking-Konert, C., Bettinger, D., Par, G., Thimme, R., Cantagrel, A., Lohse, A. W., Wedemeyer, H., de Man, R. & Mallet, V., 22.02.2019, in : **VIRUSES-BASEL**. 11, 2 (last impact factor 4.05)
 - **Detection of a Broad Range of Low-Level Major Histocompatibility Complex Class II-Restricted, Hepatitis Delta Virus (HDV)-Specific T-Cell Responses Regardless of Clinical Status**
Landahl, J., Bockmann, J. H., Scheurich, C., Ackermann, C., Matzat, V., Heide, J., Nuurei, T., D'Antonio, G., **von Felden, J.**, Sette, A., Peine, S., Lohse, A. W., Lütgehetmann, M., Marget, M., Sidney, J. & Schulze Zur Wiesch, J., 29.01.2019, in : **J INFECT DIS**. 219, 4, S. 568-577 10 S. (last impact factor 5.23)
 - **Genetic variants in PNPLA3 and TM6SF2 predispose to the development of hepatocellular carcinoma in individuals with alcohol-related cirrhosis**
Stickel, F., Buch, S., Nischalke, H. D., Weiss, K. H., Gotthardt, D., Fischer, J., Rosendahl, J., Marot, A., Elamly, M., Casper, M., Lammert, F., McQuillin, A., Zopf, S., Spengler, U., Marhenke, S., Kirstein, M. M., Vogel, A., Eyer, F., **von Felden, J.**, Wege, H., Buch, T., Schafmayer, C., Braun, F., Deltenre, P., Berg, T., Morgan, M. Y. & Hampe, J., 10.2018, in : **AM J GASTROENTEROL**. 113, 10, S. 1475-1483 9 S. (last impact factor 10.86)
 - **High-density single cell mRNA sequencing to characterize circulating tumor cells in hepatocellular carcinoma**
D'Avola, D., Villacorta-Martin, C., Martins-Filho, S. N., Craig, A., Labgaa, I., **von Felden, J.**, Kimaada, A., Bonaccorso, A., Tabrizian, P., Hartmann, B. M., Sebra, R., Schwartz, M. & Villanueva, A., 01.08.2018, in : **SCI REP-UK**. 8, S. 11570 (last impact factor 4.38)
 - **A pilot study of ultra-deep targeted sequencing of plasma DNA identifies driver mutations in hepatocellular carcinoma**
Labgaa, I., Villacorta-Martin, C., D'Avola, D., Craig, A. J., **von Felden, J.**, Martins-Filho, S. N., Sia, D., Stueck, A., Ward, S. C., Fiel, M. I., Mahajan, M., Tabrizian, P., Thung, S. N., Ang, C., Friedman, S. L., Llovet, J. M., Schwartz, M. & Villanueva, A., 07.2018, in : **ONCOGENE**. 37, 27, S. 3740-3752 13 S. (last impact factor 9.87)
 - **Usefulness of biochemical remission and transient elastography in monitoring disease course in autoimmune hepatitis**
Hartl, J., Ehken, H., Sebode, M., Peiseler, M., Krech, T., Zenouzi, R., **von Felden, J.**, Weiler-Normann, C., Schramm, C. & Lohse, A. W., 04.2018, in : **J HEPATOL**. 68, 4, S. 754-763 10 S., 4. (last impact factor 25.08)
 - **Levels of Cytokines in Serum Associate With Development of Hepatocellular Carcinoma in Patients With HCV Infection Treated With Direct-Acting Antivirals**
Debes, J. D., van Tilborg, M., Groothuisink, Z. M. A., Hansen, B. E., Schulze Zur Wiesch, J., **von Felden, J.**, de Knegt, R. J. & Boonstra, A., 02.2018, in : **GASTROENTEROLOGY**. 154, 3, S. 515-517 (last impact factor 22.68)