

## **ESP Advanced Training Center for Pancreatobiliary Pathology**

- **Name of the center and address:**

Institute of Pathology

University Hospital of Duesseldorf

Moorenstrasse 5

40225, Duesseldorf

Germany

- **Chair of the Center:**

Prof. Dr. Irene Esposito

- **Head of the training programme:**

Prof. Dr. Irene Esposito

- **Trainers**

Prof. Dr. Irene Esposito

Dr. Aslihan Yavas

Dr. Lena Haeberle

Dr. Martin Schramm (cytopathology)

- **Details about specific areas in which training can be offered:**

### Pancreatobiliary pathology

Pancreatobiliary pathology is one of the most challenging areas of diagnostic pathology. Due to the limited number of high-volume centers performing pancreatobiliary surgery, the complex anatomy of the resection specimens and the variety of neoplastic and non-neoplastic diseases involving these organs, pancreatobiliary pathology requires a highly experienced and dedicated staff. The University Hospital of Duesseldorf is one of the largest medical centers of Nordrhein-Westfalia, the most populated region of Germany and is member of the Center for Integrative Oncology Aachen- Bonn- Cologne- Duesseldorf (CIO-ABCD; <https://krebszentrum-cio.de/>). The Institute of Pathology at the University Hospital of Duesseldorf provides histopathologic, cytologic and molecular-pathological diagnostics and is one of the leading departments in Germany for the diagnostic of pancreatic and biliary neoplasia, being involved in clinical studies, in the development of interdisciplinary guidelines for diagnostic and therapy and in educational activities in this field. In addition, the University Hospital of Düsseldorf is member of the German Network for Personalized Medicine and utilizes precision medicine with personalized therapy

options and up-to-date molecular pathology by analyzing molecular therapy targets in different tumor entities by next generation sequencing (NGS)-based methods.

Training program:

- Participation in processing/reporting of daily routine cases (grossing, histopathology)
- Participation in reporting of second-opinion cases
- Participation in immunohistochemical and molecular analyses
- Microscopy of case collection (n>200) of pancreatic and biliary pathology cases under guidance with particular focus on preinvasive lesions
- Pancreatobiliary cytopathology training
- Participation in morphology-based research project on pancreatobiliary diseases
- Research in progress meeting and journal Club (1h weekly)
- Participation in regular interdisciplinary meetings (2 h weekly)
- Molecular tumor board with CIO-ABCD (1 h weekly)

- **Number of positions offered for each year:**

The institution offers 1 trainee position per year for a duration of 3-6 months.

**Specific periods of the year when the visit may be realized:**

The training can start at any time during the year except middle December- middle January and July-August.

- **Other conditions:**

The institution will assist the trainee in finding an accommodation for a reasonable price, provide a letter of invitation and support in getting necessary visa, insurance or other documents if required. After completion of the training the trainee will receive a detailed certificate describing the work. Training will not be charged.

- **Contact address for requesting details:**

Dr. Aslihan Yavas

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### Prof. Irene Esposito – Publication list of the last 3 years

1. Opitz FV, Haeberle L, Daum A, **Esposito I**. Tumor Microenvironment in Pancreatic Intraepithelial Neoplasia. *Cancers (Basel)*. 2021 Dec 8;13(24):6188.
2. Valentin B, Arsov C, Ullrich T, Demetrescu D, Morawitz J, Al-Monajjed R, Quentin M, Kirchner J, **Esposito I**, Albers P, Antoch G, Schimmöller L. Comparison of 3 T mpMRI and pelvic CT examinations for detection of lymph node metastases in patients with prostate cancer. *Eur J Radiol*. 2021 Dec 17;147:110110. Epub ahead of print.
3. Wang H, Chetty R, Hosseini M, Allende DS, **Esposito I**, Matsuda Y, Deshpande V, Shi J, Dhall D, Jang KT, Kim GE, Luchini C, Graham RP, Reid MD, Basturk O, Hruban RH, Krasinskas A, Klimstra DS, Adsay V; Pancreatobiliary Pathology Society. Pathologic Examination of Pancreatic Specimens Resected for Treated Pancreatic Ductal Adenocarcinoma: Recommendations From the Pancreatobiliary Pathology Society. *Am J Surg Pathol*. 2021 Dec 10. Epub ahead of print.
4. Franken A, Behrens B, Reinhardt F, Yang L, Rivandi M, Marass F, Jaeger B, Krawczyk N, Cieslik JP, Honisch E, Asperger H, Jeannot E, Proudhon C, Beerenwinkel N, Schölermann N, **Esposito I**, Dietzel F, Stoecklein NH, Niederacher D, Fehm T, Neubauer H. Multiparametric Circulating Tumor Cell Analysis to Select Targeted Therapies for Breast Cancer Patients. *Cancers (Basel)*. 2021 Nov 29;13(23):6004.
5. Vay C, Schlünder PM, Dizdar L, **Esposito I**, Ghadimi MPH, Knoefel WT, Krieg A. Targeting abundant survivin expression in liposarcoma: subtype dependent therapy responses to YM155 treatment. *J Cancer Res Clin Oncol*. 2021 Dec 3. Epub ahead of print.
6. Sun N, Trajkovic-Arsic M, Li F, Wu Y, Münch C, Kunzke T, Feuchtinger A, Steiger K, Schlitter AM, Weichert W, **Esposito I**, Siveke JT, Walch A. Native glycan fragments detected by MALDI mass spectrometry imaging are independent prognostic factors in pancreatic ductal adenocarcinoma. *EJNMMI Res*. 2021 Dec 1;11(1):120.
7. Boschheidgen M, Schimmöller L, Arsov C, Ziayee F, Morawitz J, Valentin B, Radke KL, Giessing M, **Esposito I**, Albers P, Antoch G, Ullrich T. MRI grading for the prediction of prostate cancer aggressiveness. *Eur Radiol*. 2021 Nov 8. Epub ahead of print.
8. Fischer JC, Schmidt AG, Bölke E, Uhrberg M, Keitel V, Feldt T, Jensen B, Häussinger D, Adams O, Schneider EM, Balz V, Enczmann J, Rox J, Hermsen D, Schulze-Bosse K, Kindgen-Milles D, Knoefel WT, van Griensven M, Haussmann J, Tamaskovics B, Plettenberg C, Scheckenbach K, Corradini S, Pedoto A, Maas K, Schmidt L, Grebe O, **Esposito I**, Ehrhardt A, Peiper M, Buhren BA, Calles C, Stöhr A, Lichtenberg A, Freise NF, Lutterbeck M, Rezazadeh A, Budach W, Matuschek C. Association of HLA

genotypes, ABO blood type and chemokine receptor 5 mutant CD195 with the clinical course of COVID-19. *Eur J Med Res*. 2021 Sep 16;26(1):107.

9. Verona EBM 2020 on IPMN Consortium. Verona Evidence-Based Meeting (EBM) 2020 on Intraductal Papillary Mucinous Neoplasms (IPMNs) of the Pancreas: Meeting Report. *Dig Surg*. 2021;38(4):316-322.
10. Safi SA, Haeberle L, Heuvelde S, Kroepil P, Fung S, Rehders A, Keitel V, Luedde T, Fuerst G, **Esposito I**, Ziyee F, Antoch G, Knoefel WT, Fluegen G. Pre-Operative MDCT Staging Predicts Mesopancreatic Fat Infiltration-A Novel Marker for Neoadjuvant Treatment? *Cancers (Basel)*. 2021 Aug 28;13(17):4361.
11. Klöppel G, **Esposito I**. Die Pankreopathologie zwischen 2005 und 2021: Es geht voran! [Pancreatic pathology between 2005 and 2021: we're making progress!]. *Pathologe*. 2021 Sep;42(5):451-452. German.
12. **Esposito I**, Gaida MM. Pankreopathologie [Pancreatic pathology]. *Pathologe*. 2021 Sep;42(5):449-450. German.
13. **Esposito I**, Häberle L, Yavas A, Kraft A, Gaida MM. Intraduktale Pankreasneoplasien [Intraductal neoplasms of the pancreas]. *Pathologe*. 2021 Sep;42(5):472-483. German.
14. Safi SA, Rehders A, Haeberle L, Fung S, Lehwald N, **Esposito I**, Ziyee F, Krieg A, Knoefel WT, Fluegen G. Para-aortic lymph nodes and ductal adenocarcinoma of the pancreas: Distant neighbors? *Surgery*. 2021 Dec;170(6):1807-1814.
15. Verbeke C, Webster F, Brosens L, Campbell F, Del Chiaro M, **Esposito I**, Feakins RM, Fukushima N, Gill AJ, Kakar S, Kench JG, Krasinskas AM, van Laethem JL, Schaeffer DF, Washington K. Dataset for the reporting of carcinoma of the exocrine pancreas: recommendations from the International Collaboration on Cancer Reporting (ICCR). *Histopathology*. 2021 Dec;79(6):902-912.
16. Schlitter AM, Häberle L, Richter C, Huss R, **Esposito I**. Standardisierte Befundung des Pankreaskopfkarcinoms [Standardized diagnosis of pancreatic head carcinoma]. *Pathologe*. 2021 Sep;42(5):453-463. German.
17. Häberle L, Schramm M, **Esposito I**. Punktionsdiagnostik von Pankreasneoplasien [Preoperative diagnostics of pancreatic neoplasms]. *Pathologe*. 2021 Sep;42(5):491-500. German.
18. Gross C, Engleitner T, Lange S, Weber J, Jesinghaus M, Konukiewitz B, Muckenhuber A, Steiger K, Pfarr N, Goepfert B, Keller G, Weichert W, Adsay NV, Klöppel G, Rad R,

**Esposito I**, Schlitter AM. Whole Exome Sequencing of Biliary Tubulopapillary Neoplasms Reveals Common Mutations in Chromatin Remodeling Genes. *Cancers (Basel)*. 2021 Jun 1;13(11):2742.

19. Klindt C, Jensen BE, Brandenburger T, Feldt T, Killer A, Schimmöller L, Antoch G, Senff T, Hauka S, Timm J, Bahnert BH, Seidl M, **Esposito I**, Luedde T, Bode JG, Keitel V. Secondary sclerosing cholangitis as a complication of severe COVID-19: A case report and review of the literature. *Clin Case Rep*. 2021 May 24;9(5):e04068.
20. Griesmann H, Mühl S, Riedel J, Theuerkorn K, Sipos B, **Esposito I**, Vanden Heuvel GB, Michl P. CUX1 Enhances Pancreatic Cancer Formation by Synergizing with KRAS and Inducing MEK/ERK-Dependent Proliferation. *Cancers (Basel)*. 2021 May 18;13(10):2462.
21. Haeberle L, Busch M, Kirchner J, Fluegen G, Antoch G, Knoefel WT, **Esposito I**. Pancreatic ductal adenocarcinoma concomitant with pancreatic metastases of clear-cell renal cell carcinoma: a case report. *J Med Case Rep*. 2021 May 31;15(1):314.
22. Reich M, Spomer L, Klindt C, Fuchs K, Stindt J, Deutschmann K, Höhne J, Liaskou E, Hov JR, Karlsen TH, Beuers U, Verheij J, Ferreira-Gonzalez S, Hirschfield G, Forbes SJ, Schramm C, **Esposito I**, Nierhoff D, Fickert P, Fuchs CD, Trauner M, García-Beccaria M, Gabernet G, Nahnsen S, Mallm JP, Vogel M, Schoonjans K, Lautwein T, Köhrer K, Häussinger D, Luedde T, Heikenwalder M, Keitel V. Downregulation of TGR5 (GPBAR1) in biliary epithelial cells contributes to the pathogenesis of sclerosing cholangitis. *J Hepatol*. 2021 Sep;75(3):634-646.
23. Safi SA, Haeberle L, Fluegen G, Lehwald-Tywuschik N, Krieg A, Keitel V, Luedde T, **Esposito I**, Rehders A, Knoefel WT. Mesopancreatic excision for pancreatic ductal adenocarcinoma improves local disease control and survival. *Pancreatology*. 2021 Jun;21(4):787-795.
24. Haeberle L, Cacciato Insilla A, Kapp AC, Steiger K, Schlitter AM, Konukiewicz B, Demir IE, Friess H, **Esposito I**. Stroma composition and proliferative activity are related to therapy response in neoadjuvant treated pancreatic ductal adenocarcinoma. *Histol Histopathol*. 2021 Jul;36(7):733-742.
25. Heydt C, Wölwer CB, Velazquez Camacho O, Wagener-Rydzek S, Pappesch R, Siemanowski J, Rehker J, Haller F, Agaimy A, Worm K, Herold T, Pfarr N, Weichert W, Kirchner T, Jung A, Kumbrink J, Goering W, **Esposito I**, Buettner R, Hillmer AM, Merkelbach-Bruse S. Detection of gene fusions using targeted next-generation sequencing: a comparative evaluation. *BMC Med Genomics*. 2021 Feb 27;14(1):62.

26. Klingebiel M, Arsov C, Ullrich T, Quentin M, Al-Monajjed R, Mally D, Sawicki LM, Hiester A, **Esposito I**, Albers P, Antoch G, Schimmöller L. Reasons for missing clinically significant prostate cancer by targeted magnetic resonance imaging/ultrasound fusion-guided biopsy. *Eur J Radiol.* 2021 Apr;137:109587.
27. Liebe R, **Esposito I**, Bock HH, Vom Dahl S, Stindt J, Baumann U, Luedde T, Keitel V. Diagnosis and management of secondary causes of steatohepatitis. *J Hepatol.* 2021 Jun;74(6):1455-1471.
28. Haeberle L, Schramm M, Goering W, Frohn L, Driescher C, Hartwig W, Preissinger-Heinzel HK, Beyna T, Neuhaus H, Fuchs K, Keitel-Anselmino V, Knoefel WT, **Esposito I**. Molecular analysis of cyst fluids improves the diagnostic accuracy of pre-operative assessment of pancreatic cystic lesions. *Sci Rep.* 2021 Feb 3;11(1):2901.
29. **Esposito I**, Haeberle L. Nonmucinous Cystic Lesions of the Pancreas. *Arch Pathol Lab Med.* 2021 Jan 27.
30. Goepfert B, Stichel D, Toth R, Fritzsche S, Loeffler MA, Schlitter AM, Neumann O, Assenov Y, Vogel MN, Mehrabi A, Hoffmann K, Köhler B, Springfield C, Weichenhan D, Plass C, **Esposito I**, Schirmacher P, von Deimling A, Roessler S. Integrative analysis reveals early and distinct genetic and epigenetic changes in intraductal papillary and tubulopapillary cholangiocarcinogenesis. *Gut.* 2021 Jan 19;gutjnl-2020-322983.
31. Stabinska J, Ljimini A, Zöllner HJ, Wilken E, Benkert T, Limberg J, **Esposito I**, Antoch G, Wittsack HJ. Spectral diffusion analysis of kidney intravoxel incoherent motion MRI in healthy volunteers and patients with renal pathologies. *Magn Reson Med.* 2021 Jun;85(6):3085-3095.
32. Valentin B, Schimmöller L, Ullrich T, Klingebiel M, Demetrescu D, Sawicki LM, Lakes J, Mally D, Quentin M, **Esposito I**, Albers P, Antoch G, Arsov C. Magnetic resonance imaging improves the prediction of tumor staging in localized prostate cancer. *Abdom Radiol (NY).* 2021 Jun;46(6):2751-2759.
33. Babaryka G, Janßen S, Winand E, Häberle L, **Esposito I**. Dusseldorf autopsies 1914-1918. *Virchows Arch.* 2021 Jun;478(6):1187-1195.
34. Driescher C, Fuchs K, Haeberle L, Goering W, Frohn L, Opitz FV, Haeussinger D, Knoefel WT, Keitel V, **Esposito I**. Bile-Based Cell-Free DNA Analysis Is a Reliable Diagnostic Tool in Pancreatobiliary Cancer. *Cancers (Basel).* 2020 Dec 25;13(1):39.
35. Morawitz J, Kirchner J, Martin O, Bruckmann NM, Dietzel F, Li Y, Rischpler C, Herrmann K, Umutlu L, Bittner AK, Mohrmann S, Ingenwerth M, Häberle L, **Esposito I**, Antoch G, Buchbender C, Sawicki LM. Prospective Correlation of Prognostic

Immunohistochemical Markers With SUV and ADC Derived From Dedicated Hybrid Breast 18F-FDG PET/MRI in Women With Newly Diagnosed Breast Cancer. *Clin Nucl Med*. 2021 Mar 1;46(3):201-205.

36. Karamitopoulou E, **Esposito I**, Zlobec I, Insilla AC, Wartenberg M, Schaeffer DF, Kalloger S, La Rosa S, Sempoux C, Ramos Centeno I, Lohneis P. Reproducibility of tumor budding assessment in pancreatic cancer based on a multicenter interobserver study. *Virchows Arch*. 2021 Apr;478(4):719-726.
37. Osses DF, Arsov C, Schimmöller L, Schoots IG, van Leenders GJLH, **Esposito I**, Remmers S, Albers P, Roobol MJ. Equivocal PI-RADS Three Lesions on Prostate Magnetic Resonance Imaging: Risk Stratification Strategies to Avoid MRI-Targeted Biopsies. *J Pers Med*. 2020 Dec 10;10(4):270.
38. Apostolopoulou M, Gordillo R, Gancheva S, Strassburger K, Herder C, **Esposito I**, Schlensak M, Scherer PE, Roden M. Role of ceramide-to-dihydroceramide ratios for insulin resistance and non-alcoholic fatty liver disease in humans. *BMJ Open Diabetes Res Care*. 2020 Nov;8(2):e001860.
39. Janssen BV, Tutucu F, van Roessel S, Adsay V, Basturk O, Campbell F, Doglioni C, **Esposito I**, Feakins R, Fukushima N, Gill AJ, Hruban RH, Kaplan J, Koerkamp BG, Hong SM, Krasinskas A, Luchini C, Offerhaus J, Sarasqueta AF, Shi C, Singhi A, Stoop TF, Soer EC, Thompson E, van Tienhoven G, Velthuisen MF, Wilmink JW, Besselink MG, Brosens LAA, Wang H, Verbeke CS, Verheij J; International Study Group of Pancreatic Pathologists (ISGPP). Amsterdam International Consensus Meeting: tumor response scoring in the pathology assessment of resected pancreatic cancer after neoadjuvant therapy. *Mod Pathol*. 2021 Jan;34(1):4-12.
40. **Esposito I**, Hruban RH, Verbeke C, Terris B, Zamboni G, Scarpa A, Morohoshi T, Suda K, Luchini C, Klimstra DS, Adsay V, Haeberle L, Saluja A, Fernandez-Del Castillo C, Sheel A, Neoptolemos JP, Isaji S, Shimosegawa T, Whitcomb DC, Campbell F; Working group for the International (IAP – APA – JPS – EPC) Consensus Guidelines for Chronic Pancreatitis. Guidelines on the histopathology of chronic pancreatitis. Recommendations from the working group for the international consensus guidelines for chronic pancreatitis in collaboration with the International Association of Pancreatology, the American Pancreatic Association, the Japan Pancreas Society, and the European Pancreatic Club. *Pancreatology*. 2020 Jun;20(4):586-593.
41. Kirchner J, Martin O, Umutlu L, Herrmann K, Bittner AK, Hoffmann O, Mohrmann S, Gauler T, Theurer S, Antke C, **Esposito I**, Kinner S, Schaarschmidt BM, Kowall B, Lütke-Brintrup D, Stang A, Becker AS, Antoch G, Buchbender C. Impact of 18F-FDG PET/MR

on therapeutic management in high risk primary breast cancer patients - A prospective evaluation of staging algorithms. *Eur J Radiol.* 2020 Jul;128:108975.

42. Morsch R, Rose M, Maurer A, Cassataro MA, Braunschweig T, Knüchel R, Vögeli TA, Ecke T, Eckstein M, Weyerer V, **Esposito I**, Ackermann M, Niegisch G, Gaisa NT; German Study Group of Bladder Cancer (DFBK e.V.). Therapeutic implications of PD-L1 expression in bladder cancer with squamous differentiation. *BMC Cancer.* 2020 Mar 18;20(1):230.
43. Kalisz M, Bernardo E, Beucher A, Maestro MA, Del Pozo N, Millán I, Haeberle L, Schlensog M, Safi SA, Knoefel WT, Grau V, de Vas M, Shpargel KB, Vaquero E, Magnuson T, Ortega S, **Esposito I**, Real FX, Ferrer J. HNF1A recruits KDM6A to activate differentiated acinar cell programs that suppress pancreatic cancer. *EMBO J.* 2020 May 4;39(9):e102808.
44. Krawczyk N, Neubacher M, Meier-Stiegen F, Neubauer H, Niederacher D, Ruckhäberle E, Mohrmann S, Hoffmann J, Kaleta T, Banys-Paluchowski M, Reinecke P, **Esposito I**, Janni W, Fehm T. Determination of the androgen receptor status of circulating tumour cells in metastatic breast cancer patients. *BMC Cancer.* 2019 Nov 12;19(1):1101.
45. Franken A, Honisch E, Reinhardt F, Meier-Stiegen F, Yang L, Jaschinski S, **Esposito I**, Alberter B, Polzer B, Huebner H, Fasching PA, Pancholi S, Martin LA, Ruckhäberle E, Schochter F, Tzschaschel M, Hartkopf AD, Mueller V, Niederacher D, Fehm T, Neubauer H. Detection of ESR1 Mutations in Single Circulating Tumor Cells on Estrogen Deprivation Therapy but Not in Primary Tumors from Metastatic Luminal Breast Cancer Patients. *J Mol Diagn.* 2020 Jan;22(1):111-121.
46. Ortiz-Brüchle N, Muders M, Toma M, **Esposito I**, Hartmann A, Stöhr R, Reis H, Wild P, Köllermann J, Bremmer F, Leichsenring J, Stenzinger A, Merkelbach-Bruse S, Kirfel S, Perner S, Hartmann N, Roth W, Jung A, Kirchner T, Schwamborn K, Pfarr N, Dahl E, Knüchel R, Gaisa NT. [Status of the availability and use of next generation sequencing (NGS) in bladder cancer-a questionnaire within the uropathology working group]. *Urologe A.* 2020 Mar;59(3):318-325.
47. Haeberle L, **Esposito I**. Pathology of pancreatic cancer. *Transl Gastroenterol Hepatol.* 2019 Jun 27;4:50.
48. Kersting D, Fasbender S, Pilch R, Kurth J, Franken A, Ludescher M, Naskou J, Hallenberger A, Gall CV, Mohr CJ, Lukowski R, Raba K, Jaschinski S, **Esposito I**, Fischer JC, Fehm T, Niederacher D, Neubauer H, Heinzel T. From in vitro to ex vivo: subcellular localization and uptake of graphene quantum dots into solid tumors. *Nanotechnology.* 2019 Sep 27;30(39):395101.

49. Benitz S, Straub T, Mahajan UM, Mutter J, Czernel S, Unruh T, Wingerath B, Deubler S, Fahr L, Cheng T, Nahnsen S, Bruns P, Kong B, Raulefs S, Ceyhan GO, Mayerle J, Steiger K, **Esposito I**, Kleeff J, Michalski CW, Regel I. Ring1b-dependent epigenetic remodelling is an essential prerequisite for pancreatic carcinogenesis. *Gut*. 2019 Nov;68(11):2007-2018.
50. Regel I, Raulefs S, Benitz S, Mihaljevic C, Rieder S, Leinenkugel G, Steiger K, Schlitter AM, **Esposito I**, Mayerle J, Kong B, Kleeff J, Michalski CW. Loss of TLR3 and its downstream signaling accelerates acinar cell damage in the acute phase of pancreatitis. *Pancreatol*. 2019 Jan;19(1):149-157.