# 45P Deep learning model identifies lynch syndrome versus sporadic MSI-H from adenoma histology [Abstract]

**S. Sainath, Nic G. Reitsam, K. Papadopoulou, M. Kloor, J. Nattermann, G. Raptou, K. Petraki, E. Papadopoulou, A. Eliades, J. I. Sgouros, G. Papaxoinis, S. Pervana, G. Fountzilas, G. Pentheroudakis, D. G. Pectasides, G. Koumbaris, R. Hueneburg, E. Fountzilas, J. Nikolas Kather**

**Angaben zur Veröffentlichung / Publication details:**

Sainath, S., Nic G. Reitsam, K. Papadopoulou, M. Kloor, J. Nattermann, G. Raptou, K. Petraki, et al. 2025. "45P Deep learning model identifies lynch syndrome versus sporadic MSI-H from adenoma histology [Abstract]." *ESMO Real World Data and Digital Oncology* 10 (Supplement): 100244. https://doi.org/10.1016/j.esmorw.2025.100244.

## 45P Deep learning model identifies lynch syndrome versus sporadic MSI-H from adenoma histology

S. Sainath[1], N.G. Reitsam[2], K. Papadopoulou[3], M. Kloor[4], J. Nattermann[5], G. Raptou[6], K. Petraki[7], E. Papadopoulou[8], A. Eliades[9], J.I. Sgouros[10], G. Papaxoinis[11], S. Pervana[12], G. Fountzilas[13], G. Pentheroudakis[14], D.G. Pectasides[15], G. Koumbaris[16], R. Hueneburg[17], E. Fountzilas[18], J. Nikolas Kather[19]

[1]*Department of Digital Health, EKFZ - Else Kröner Fresenius Zentrum für Digitale Gesundheit, Dresden, Germany;* [2]*Pathology & Molecular Diagnostics Department Universitätsklinikum Augsburg, Augsburg, Germany;* [3]*Lab of Molecular Oncology, HeCOG - Hellenic Cooperative Oncology Group, Athens, Greece;* [4]*Applied Tumor Biology, University Hospital Heidelberg, Institute of Pathology, Heidelberg, Germany;* [5]*Department of Internal Medicine I, University Hospital Bonn, Bonn, Germany;* [6]*Department of Pathology, Aristotle University of Thessaloniki, Thessaloniki, Greece;* [7]*Pathology Department, HeCOG - Hellenic Cooperative Oncology Group, Athens, Greece;* [8]*Scientific and clinical team, Genekor SA, Gerakas, Greece;* [9]*Medicover Genetics Ltd, Medicover Genetics Ltd, Nicosia, Cyprus;* [10]*Third Department of Medical Oncology, General Oncology Hospital of Kifissia Agioi Anargyroi, Kifisia, Greece;* [11]*2nd Department of Medical Oncology, "Agios Savvas" - Anticancer Hospital, Athens, Greece;* [12]*Department of Pathology, HeCOG - Hellenic Cooperative Oncology Group, Athens, Greece;* [13]*Laboratory of Molecular Oncology, Aristotle University of Thessaloniki - School of Medicine, Thessaloniki, Greece;* [14]*Scientific and Medical Division, ESMO - European Society for Medical Oncology, Lugano, Switzerland;* [15]*2nd Department of Internal Medicine, Hippokration General Hospital, Athens, Greece;* [16]*MEDICOVER Genetics, Medicover Genetics Ltd, Engomi, Cyprus;* [17]*Medizinische Klinik und Poliklinik I, UKB - Universitätsklinikum Bonn, Bonn, Germany;* [18]*Department of Medical Oncology, St Luke's Hospital-Agios Loukas Clinic, Thessaloniki, Greece;* [19]*EKFZ - Digital Health, TU Dresden, Carl Gustav Carus Campus, Dresden, Germany*

**Background:** Lynch syndrome (LS) is the most common hereditary colorectal cancer (CRC), affecting up to 1 in 300 individuals with lifetime CRC risks >60% and high rates of metachronous cancers. Early recognition is essential for surveillance and preventive care, ideally before manifest cancer develops, yet germline testing is costly and not universally accessible. While both LS and sporadic microsatellite instability-high (MSI-H) cancers share molecular features, they arise from distinct precursors, conventional adenomas versus serrated polyps, suggesting that adenoma morphology may provide clinically useful, though not definitive, signals for differentiation. We hypothesised that such features can be detected by deep learning (DL) models on routine histology slides.

**Methods:** We trained a transformer-based deep learning (DL) model on Haematoxylin and Eosin (H&E)-stained whole slide image (WSI) features (using VIRCHOW-2) to distinguish LS from sporadic cases. The training cohort comprised 298 WSIs from 297 adenoma patients (120 LS, 177 sporadic) from Bonn, Germany. Generalisability was tested on an external MSI-H CRC cohort from the Hellenic Cooperative Oncology Group (HeCOG), Greece ($n = 164$; 27 LS, 137 sporadic; 176 WSIs).

**Results:** In 3-fold cross-validation, the model achieved a mean area under the receiver operating characteristic curve (AUROC) of 0.92 [0.91—0.94] and mean area under the precision-recall curve (AUPRC) of 0.95 [0.95—0.95] for classifying sporadic cases ($p < 0.001$). Despite being trained only on adenomas, the model achieved a mean AUROC of 0.73 [0.66—0.79] and mean AUPRC of 0.92 [0.89—0.95] for sporadic classification ($p < 0.001$) on the external MSI-H CRC cohort, suggesting morphological signals persist in carcinomas. Explainability analysis using heatmaps, top tiles, and pathology review suggests the model may detect subtle patterns like lymphocyte-rich mucosa in LS adenomas. Though subtle features remain hard to interpret, the DL model's ability to identify them indicates they warrant deeper analysis.

**Conclusions:** Our findings demonstrate that an H&E-based DL model trained on adenomas can effectively differentiate LS from sporadic MSI-H CRC, supporting a scalable and affordable histopathology-based approach to LS screening.

**Editorial acknowledgement:** During the preparation of this work the author(s) used ChatGPT (GPT-4o) in order to rephrase sentences inorder to limit the character count within 2000. After using this tool/service, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the publication.

**Legal entity responsible for the study:** EKFZ für Digitale Gesundheit, Medizinische Fakultät der TU Dresden.

**Funding:** DEEP-HCC, 031L0315A.

**Disclosure:** N.G. Reitsam: Financial Interests, Institutional, Invited Speaker: Bruker (Formerly Nanostring). E. Fountzilas: Financial Interests, Personal, Advisory Role: Amgen; Financial Interests, Personal, Other, Travel Grant: Pfizer, Genesis; Financial Interests, Personal, Invited Speaker, Travel Grant: AstraZeneca; Financial Interests, Personal, Invited Speaker: Lilly, GSK; Financial Interests, Personal, Stocks/Shares: Genprex Inc., Deciphera Pharmaceuticals, Inc.. J. Nikolas Kather: Financial Interests, Personal, Other, Consulting: Panakeia, MultiplexDx, Mindpeak, Owkin, DoMore Diagnostics, Bioptimus; Financial Interests, Personal, Other, Consulting, honoraria: AstraZeneca; Financial Interests, Personal, Stocks/Shares: StratifAI, Synagen, Tremont AI, Ignition Labs; Financial Interests, Institutional, Other, Institutional research grant: GSK; Financial Interests, Personal, Other, Honoraria: Bayer, Daiichi Sankyo, Eisai, Janssen, Merck, MSD, BMS, Roche, Pfizer, Fresenius. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.esmorw.2025.100244