

## HABILITATION THESIS REVIEWER'S REPORT

### Masaryk University

**Applicant**

Dr. Eva Budinska, Ph.D.

**Habilitation thesis**

Integrative Bioinformatics and Computational Modelling in Colorectal Cancer: Unveiling Tumor Heterogeneity through Multi-Omics Data

**Reviewer**

Prof. Olivier Michielin, MD-PhD

**Reviewer's home unit, institution**

Geneva University Hospital

The habilitation thesis submitted by Dr. Eva Budinska presents an extensive body of work dedicated to the understanding of colorectal cancer (CRC) heterogeneity through integrative computational biology and translational oncology approaches. The thesis is based on a substantial collection of high-quality publications that collectively illustrate both methodological innovation and clinically relevant biological insights. This high level of methodological development and data integration in a sound clinical context with clear patient oriented objectives is rare and should be saluted.

One of the major strengths of this work lies in its genuinely integrative nature. Dr. Budinska successfully combines transcriptomics, histopathological image analysis, microbiome characterization, and computational modelling into a unified framework aimed at deciphering tumour complexity. Importantly, the thesis goes beyond purely descriptive bioinformatics and consistently seeks biological interpretation and translational applicability towards the patient.

A particularly noteworthy aspect is the candidate's contribution to the refinement of CRC molecular stratification. By developing and applying robust computational classifiers and feature selection methodologies, the work contributes to improving patient subgroup identification and to advancing precision oncology approaches in colorectal cancer. The integration of multiple layers of omics information represents a technically demanding challenge, and the thesis demonstrates a high level of methodological maturity in addressing these issues.

Another important contribution concerns the analysis of spatial and morphological heterogeneity through digital pathology approaches. The linkage between histomorphological patterns and molecular phenotypes is of considerable interest in modern oncology, especially in the context of emerging AI-driven pathology tools. Dr. Budinska's work contributes to bridging these domains and highlights how computational pathology may support future diagnostic and prognostic workflows.

The thesis also demonstrates a strong awareness of the tumour microenvironment as a dynamic ecosystem rather than a purely tumour-cell intrinsic process. In this regard, the incorporation of microbiome-related analyses into CRC heterogeneity studies is particularly innovative and timely. These investigations may ultimately contribute to improved understanding of host–tumour interactions and potentially open novel avenues for therapeutic modulation.

Importantly, the candidate consistently validates computational findings in biologically and clinically relevant systems, including patient-derived material and preclinical models. This translational orientation significantly strengthens the overall scientific impact of the work. The use of genetically engineered mouse models and xenograft systems not merely as experimental tools but as platforms for cross-validation of molecular classifications further underscores the rigor of the approach.

Beyond the individual scientific contributions, the thesis reflects the profile of an independent investigator capable of operating at the interface between computational sciences, molecular oncology, pathology, and translational medicine. Such interdisciplinarity is increasingly essential in modern cancer research and represents one of the strongest aspects of the candidate’s academic trajectory.

Overall, the habilitation thesis constitutes a substantial and coherent contribution to the field of computational and translational CRC oncology. The scientific quality of the presented work is very high, the methodological approaches are rigorous, and the translational relevance is clear. In my opinion, Dr. Budinska demonstrates the scientific independence, originality, and academic maturity expected for a habilitation thesis.

**Reviewer's questions for the habilitation thesis defence** (number of questions up to the reviewer)

1. Multi-omics integration approaches often face challenges related to reproducibility and standardization across datasets and institutions. Which methodological strategies do you consider most critical to ensure robustness and clinical transferability of integrative CRC classifiers?
2. Could digital pathology be at risk of lacking transferability from one hospital to another? What would be the ways to mitigate this risk?
3. As artificial intelligence and digital pathology rapidly evolve, how do you envision the future interaction between histopathological image-based biomarkers and molecular profiling in routine clinical decision-making for colorectal cancer?

**Conclusion**

The habilitation thesis entitled “Integrative Bioinformatics and Computational Modelling in Colorectal Cancer: Unveiling Tumor Heterogeneity through Multi-Omics Data” by Eva Budinska **fulfils** requirements expected of a habilitation thesis in the field of Environmental Health Sciences.

Date: 08.05.2026

Signature: