Artificial intelligence predicts the c-Kit-11 mutational status of canine cutaneous mast cell tumors through their phenotype in HE stained histological slides

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RESEARCH QUESTION

Can a deep learning algorithm (DLA) classify tumors by c-Kit-11 mutational status on HE slides?

BACKGROUND

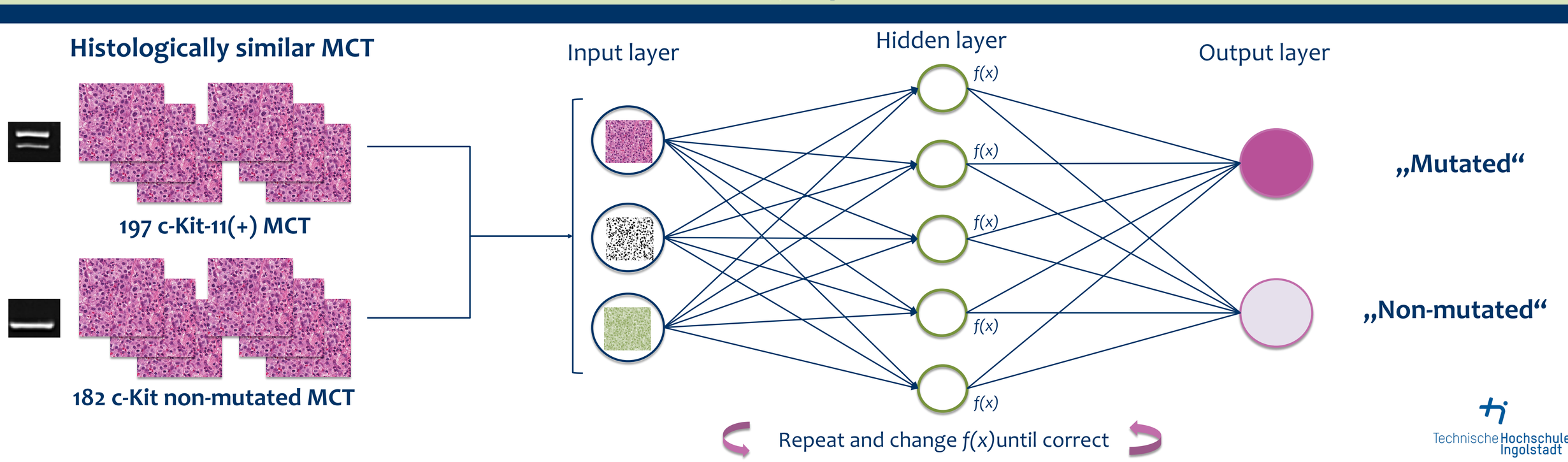
- **Mast cell tumors (MCT) are the most common skin tumor in dogs**
- Morphological prognostic factors:
  - → **Grading**
  - → AgNOR, Ki67
- Molecular prognostic factor:
  - → **c-Kit gene exon-11 mutation (PCR)**

MATERIALS AND METHODS

	C-Kit non-mutated			c-Kit-11 (+)		
	High Grade	Low Grade	**Total**	High Grade	Low Grade	**Total**
Cases (n)	97 (56,1%)	76 (43,9%)	**173 (100%)**	123 (62.4%)	74 (37.6 %)	**197 (100%)**

Cutaneous, subcutaneous and mucocutaneous MCTs were included

METHOD: weakly supervised DLA



FIRST RESULTS – Data set 1

- **Classification accuracy = 0.78**
- **AI can predict c-Kit-11 mutation**
- Extraction of diagnostic hotspots with high relevance

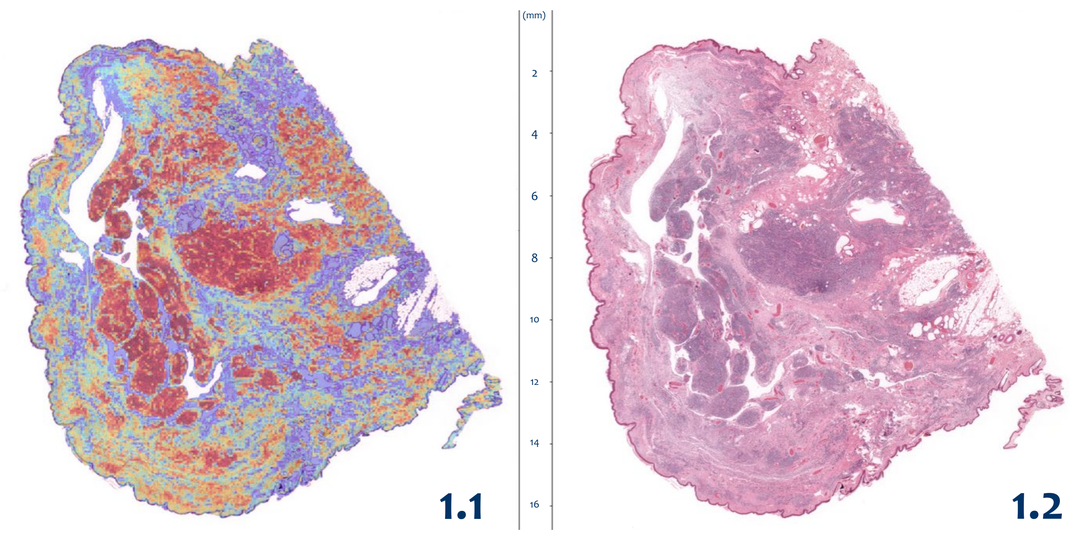
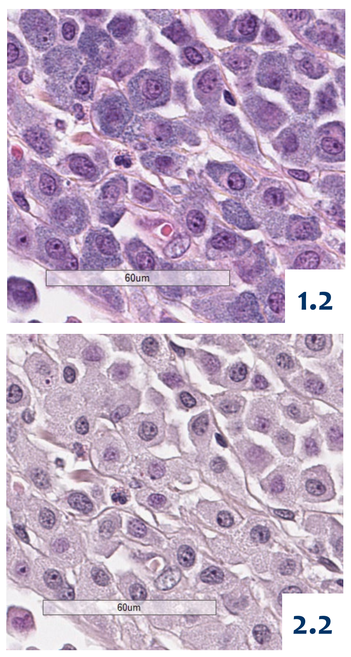


Fig. 1.1. Mutated tumor with heatmap (**Fig. 1.2**, HE stain). Heat map colors indicate area of high (red) or low (blue) relevance for prediction.

DOMAIN SHIFT

- Algorithms work best on **training environment**
- Training dataset ≠ test dataset ➔ **DOMAIN SHIFT**
- **Staining + scanner** = variables in histopathology

→ **6 different databases**



Scanner \ HE stain	A	B
1 (Aperio CS2)	1A	1B
2 (Aperio AT2)	2A	2B
3 (3DHistech Pannoramic)	3A	3B

Fig. 2.1. Non mutated MCT, stain A. Note the evident basophilic granules in the cytoplasm.
Fig 2.2. Same MCT as in Fig. 1.1., stain B. The staining is less contrasted and the cytoplasmatic granules do not appear basophilic.

SECOND RESULTS – Different datasets

Training \ Test	1A	2A	3A	1B	2B
1A	0.76	0.71	0.70	0.66	0.65
2A	0.71	0.78	0.73	0.71	0.72
3A	0.59	0.68	0.77	0.60	0.62
1B	0.65	0.73	0.62	0.78	0.74
2B	0.64	0.70	0.55	0.78	0.77

- Similar performance for all datasets **without domain shift**
- **Negative impact** of domain shift:
  - → **Scanner brand > staining**

WHAT'S NEXT

- **Identification of morphological factor(s)**
- **Mutation detection challenge** - AI vs. pathologist

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LITERATURE

- Kiupel M, Camus M. Diagnosis and Prognosis of Canine Cutaneous Mast Cell Tumors. Vet Clin North Am Small Anim Pract. 2019 Sep;49(5):819-836.
- Aubreville M, Bertram C, Veta M, et al. *Quantifying the Scanner-Induced Domain Gap in Mitosis Detection*; 2021