Introduction

Mutation of the BRAF gene
- Common cause of tumor formation in humans
  - Cellular proliferation and dedifferentiation
- Study of Mochizuki et al. (2015a+b) in the USA: BRAF variant V595E (syn. V450E) in ca. 85% of the canine transitional cell carcinomas (TCC) (PLoS ONE 2015a, 10(6):e0129534; PLoS ONE 2015b, 10(12):e0144170)

Dog population and Methods
- 57 Dogs: 0,5-17 years of age (median 10 years)
- Material: 42 biopsies
  - 46 urine samples
  - 31 cytological smears
- Diagnoses: 29 x transitional cell carcinoma
  - 20 x cystitis
  - 5 x urinary bladder polyp
  - 3 x various other lesions
- Routine cytology and histology:
  - for example: cell count of the smear, TCC grading
- Molecular genetics:
  - DNA-isolation with commercially available test kits
  - Sanger Sequencing of BRAF Variante c.1784T>A

Discussion

• The BRAF-mutation analysis on routinely submitted samples (biopsies, cytological smears, urine) was established.
• Requirement: sufficient numbers of transitional epithelial cells in the submitted material is necessary.
• Indications for BRAF-mutation analysis: 1) Non-invasive diagnostic method preferred
  2) Cytologically or histologically poor quality of material or questionable dysplastic appearance of epithelial cells
• The specificity is around 100%, since the BRAF-mutation was absent in all samples from dogs without TCC.
  - A positive result is confirming the diagnosis of TCC (or possibly prostate carcinoma, which can also show this mutation).
• Absence of the mutation interpretation: 1) Absence of a transitional cell carcinoma (for example: presence of a polyp or cystitis)
  2) Mutated transitional epithelial cells were absent in the submitted material (depending on sample size/representativity)
  3) The present TCC was not caused by a BRAF-gene mutation
  - A negative result does not rule out the presence of a transitional cell carcinoma!
• Prospect:
  1) Use of the test for early detection of TCC in urine
  2) Prognostic and therapeutic relevance of the BRAF-mutation (for example: MAPKinase inhibitors)