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ADVANCING EQUITABLE CANCER CARE THROUGH INNOVATION

Image-Based Detection of *FGFR3*-Mutations & Fusion in Urothelial Bladder Cancer

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Introduction

- Fibroblast Growth Factor Receptor 3 (*FGFR3*) is a prognostic, predictive and therapeutic target in Urothelial Bladder Cancer (UC).

- *FGFR3* alterations are found in ~15-30% of UC cases.
- Mutations occur in 12-80% of cases (depending on grade and stage).
- Fusions are less frequent, with *TACC3* being the most common partener and found in 2-6% of UC.

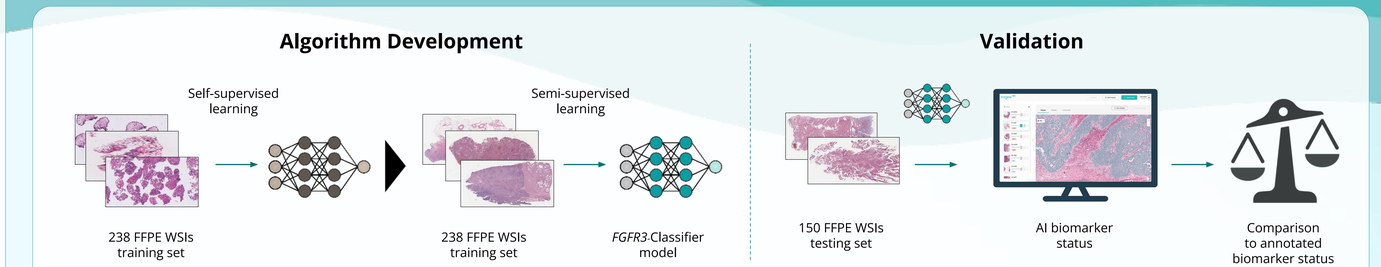
- Erdafitinib is an *FGFR2/3* kinase inhibitor used to treat advanced stages UC patients:
  - Approved indications include point mutations in *FGFR3* (R248C, S249C, G370C, Y373C) and *FGFR3-TACC3* fusions.
  - Response rate is significantly higher in patients carrying mutations compared to those with fusions.

Aim

To develop and validate image-based model for the detection of *FGFR3* alterations directly from routine pathology Hematoxylin and Eosin (H&E) scanned slides, using deep learning (DL) algorithms.

Method

- 388 H&E whole slide images (WSIs) of UC samples, obtained from the TCGA Research Network (https://www.cancer.gov/tcga) were used.
- Cases were randomly divided into training (n=238) and testing (n=150) sets.
- Advanced Convolutional Neural Network (CNN) was used to generate the *FGFR3*-Classifier on the training set following validation on the testing set.



Results

- Validation of the *FGFR3*-Classifier was performed on 150 cases from 19 different centers.
- The cohort included a total of 20 positive cases (17 actionable *FGFR3* mutations and 3 *FGFR3-TACC3* fusion cases).
- The *FGFR3*-Classifier performance was measured in comparison to the TCGA dataset annotations.

	Official Results		*FGFR3*-Classifier Results				*FGFR3*-Classifier Performance			
Total	**P**	**N**	**TP**	**TN**	**FP**	**FN**	**Sensitivity**	**Specificity**	**Accuracy**	**AUC**
n=150	20	130	19	111	19	1	95%	85.4%	86.7%	0.93

P- Positive, N- Negative, TP- true positive, TN- true negative, FP- false positive, FN- false negative, AUC- area under curve

Conclusion

- Herein, we described an AI-based solution for *FGFR3* alterations (mutations and fusions) identification in Urothelial Cancer.

- Integration of such a solution into the routine pathological pipeline can facilitate accurate, fast and systemic screening of UC patients, to support treatment optimization.

- This AI-based solution can predict biomarker status directly from H&E stained slide images, without the need for any additional tissue.

- Utilization of such an AI-based tool can support real-time molecular analysis of different types of alterations in cancers originating from a wide range of organs.