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Next-generation sequencing reveals multiple *ATM* gene variants in urothelial bladder cancer

Dimitar Ugrinovski[1,2], Slavica Josifovska[1], Kiril Pakovski[1], Saidi Skender[3], Panov Sasho[1]

[1]Laboratory for Molecular Biology and Genomics, Faculty of Natural Sciences and Mathematics, Ss. Cyril and Methodius University in Skopje, N. Macedonia, [2]PathoNext GmbH, Leipzig, Germany, [3]Urology Clinic, Medical Faculty, SS. Cyril and Methodius University in Skopje, N. Macedonia

BACKGROUND:

Urothelial bladder cancer (UBC) is the most common urinary malignancy and the tenth most diagnosed cancer worldwide. Depending on the muscle infiltration, UBC can be classified as muscle-invasive bladder cancer (MIBC) and non-muscle invasive bladder cancer (NMIBC). Based on its heterogeneity, comprehensive genomic studies reveal significant molecular differences.

MATERIAL AND METHODS:

The study included 32 patients with bladder cancer, 13 with MIBC and 19 with NMIBC. Genomic DNA was extracted from fresh frozen tumor samples and sequenced by NextSeq (Illumina) using customized panel of 95 genes. Only the pathogenic, likely pathogenic and variants of unknown significance were evaluated.

RESULTS:

The most frequently affected genes, present in ≥12% of the samples are:
TP53 (44%), *FGFR3* (41%), *PIK3CA* (34%), *STAG2* (19%), *ATM* (16%), *ERBB2* (16%), *APC* (12%), *BRAF* (12%), *KRAS* (12%) and *TERT* promoter (12%). The result is in line with the previously proposed molecular stratification by mutations in *TP53/MDM2* pathway, *FGFR3*, and *RAS* genes.
Interestingly, we observed *ATM* variants in five samples (26%) of the NIMBC, but none in the MIBC subgroup. In two samples we detected single variants (missense and frameshift deletion), while three samples had multiple variants in this gene. *ATM* plays a central role in cell division and DNA repair.

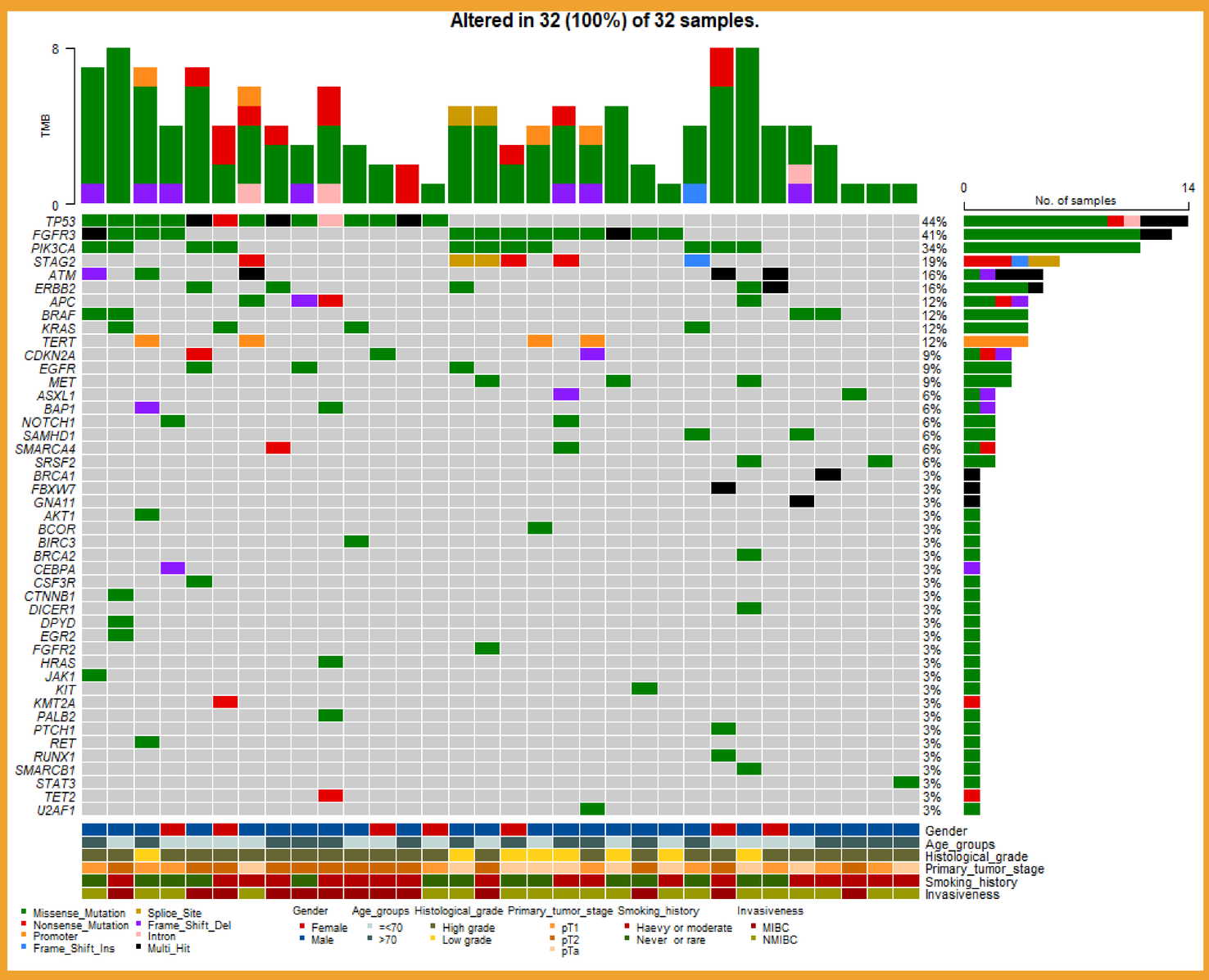

Figure 1: Oncoplot showing the distribution of mutations in the 32 patients

CONCLUSION:

Precise pathological classification together with clarification of the molecular subtype, can significantly contribute to understanding the entity of a given tumor and, especially in early stage lead to improved individualized treatment in terms of the existing and novel therapies that would target certain molecular pathways.

Presenting and corresponding author
Slavica Josifovska
josifovskas@pmf.ukim.mk

The authors declare no conflict of interest.