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Uncovering factors predicting BRAF mutation in cutaneous melanoma

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Introduction/Objective: BRAF mutations are considered to be the most common genetic alteration in cutaneous melanoma (CM). Patient management relies on assessing molecular biomarkers enabling the personalization of patients' treatment. The goal of this study was to develop the tools for predicting BRAF mutation using routine clinical and histological features.

Methods/Case Report: A total of 2041 CM cases were enrolled in the study to identify factors associated with BRAF mutation. Variables included sex, age, primary location, stage, histological type, ulceration, mitosis, Clark level, Breslow thickness, lymphocytes, lymphovascular invasion (LVI), perineural invasion (PNI), regression, microsatellite, association with nevus.

Results (if a Case Study enter NA): The Ukrainian population demonstrated a high rate of BRAF mutation in CM, associated with the younger age and location at non-sun-expose skin. This study also revealed gender-specific differences in CM anatomic distribution and BRAF mutation subtype prevalence.

By using the genetic selection method, the minimal set of variables related to BRAF mutations was defined and included age, primary tumor location, histological type, ulceration, LVI, and association with nevus. To encounter non- linear links, the non-linear neural network modeling was applied. For this aim multilayer perceptron (MLP) with one hidden layer was used. The hidden layer architecture included 4 neurons with a logistic activating function. The $AUROC_{MLP6}$ of the model was 0.79 (0.74 – 0.84). When applying the optimal threshold, the following characteristics of the model were reached: sensitivity - 89.4% (84.5 – 93.1%); specificity - 50.7% (42.2% – 59.1%); positive predictive value (PPV) - 73.1% (69.6% – 76.3%) and NPV - 76.0% (67.6% – 82.8%) respectively. The developed MLP model allows the prediction of BRAF status in CM, facilitating decisions concerning further patient management.

Conclusion: The developed MLP model, relying on 6 variables analysis allows the prediction of BRAF status in melanoma, facilitating decisions concerning further patient management.

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