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## Biomarkers In Whole Slide Images Stained By Hematoxylin-Eosin: A Groundbreaking Application Using Artificial Intelligence

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Biomarkers play a fundamental role in the diagnosis, prognosis and prediction of diseases. The study of biomarkers requires the performance of complementary diagnostic tests, which entails high costs and inevitably leads to an increase in response time, which could have a severe impact on the patient's outcome. The digital transformation in Pathology Laboratories, accompanied by the wide implementation of slide digitalization, has been decisive for the development and application of digital intelligence algorithms in a diagnostic context. The aim of this review is to assess artificial intelligence algorithms for evaluating biomarkers that can be applied to whole slide images stained by hematoxylin-eosin (WSI-HE) and to understand their advantages and limitations. There are several types of algorithms, some established on the identification and quantification of morphological biomarkers, such as nuclear density, cellular heterogeneity, the presence of certain cellular structures, tissue organization and other features. The usage of WSI-HE is enormously promising, as it reveals additional information that is not visually

observable but can help or even expand the pathologists capabilities. The identification and validation of morphological biomarkers in WSI-HE still presents challenges, such as the need for large data sets annotated using multimodal data (information from different sources, such as histopathological images, clinical data, radiological information, genomic data, among others), the interpretability of deep learning models, the integration of these biomarkers into clinical practice, among others. The application of algorithms in WSI-HE could represent an important change in patient management, contributing to timely precision medicine.

**Keywords:** Digital Pathology, Computational Pathology, Biomarkers, Whole Slide Image, Hematoxylin-Eosin