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Editorial

Immunohistochemical Expression

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1. Introduction

Immunohistochemistry (IHC) is an ancillary method, widely used in pathologist practice, that allows to identify diagnostic and prognostic/predictive therapeutic response protein markers on tissue samples by the use of specific monoclonal antibodies and chromogenic substances that guarantee the visualization of the antibody–antigene binding complex under the light microscope [1]. Coon et al. in 1941 [2] first introduced the use of fluorochrome-conjugated antibodies in clinical practice. Since then, IHC has gone from being a useful tool for identifying the differentiation line of otherwise undifferentiated cells, to a technique capable of providing not only diagnostic but also prognostic and predictive indications of response to specific therapeutic options [1,3]. The aforementioned peculiarities have made IHC one of the most used ancillary methods in the histopathological approach to human neoplastic and non-neoplastic diseases [3–5].

This Special Issue contains 11 accepted papers that provide readers with a comprehensive update on the current and future applications of IHC in medical practice.

2. Diagnostic Applications of Immunohistochemistry

The detection on tissue specimens of protein markers capable of identifying the differentiation line (melanocytic, epithelial, neural, mesenchymal or lymphoproliferative) of poorly differentiated tumors is undoubtedly one of the major advantages of IHC [3]; since its introduction, it has represented a valid diagnostic tool that, combined to the "evergreen" morphology, allowed pathologists to formulate a more accurate diagnosis of neoplasms, previously labeled as "undifferentiated" [3]. Furthermore, the increasing knowledge about the genetic landscape of human neoplasms has allowed the identification of specific genes, deriving from molecular alterations and encoding proteins, whose expression was restricted to a specific cancer type [3]; such proteins could be easily targeted by IHC, greatly improving the diagnostic accuracy of neoplasms that harbored specific molecular alterations, such as solitary fibrous tumor (SFT) [6] or glioblastoma multiforme (GBM) [7].

3. Prognostic and Predictive Value of Immunohistochemistry

However, the major clinical impact of IHC is not in the diagnostic field but that of providing the oncologist with essential prognostic and predictive information of therapeutic response [3]. The aforementioned application field of IHC was born with the introduction in clinical practice of the immunohistochemical detection of Hormone Receptors (estrogen and progesterone receptors) and HER-2/neu in the diagnostic approach to breast cancer [8,9]; in this regard, the "molecular" classification of breast cancer (Luminal A vs. Luminal B vs. HER-2/neu vs. Basal-like), based on the different combinations of Hormone Receptor and HER-2/neu immunoexpression has almost replaced the morphological one, since the former was able to select specific patient subgroups with a similar outcome and potential candidates to "personalized" treatments [8,9].

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The search for new prognostic factors, promptly identifiable by IHC, has been and still is particularly intense in the field of rare malignancies with poor prognosis. In recent years, our research group reported some immunohistochemical markers with prognostic significance in terms of overall survival, disease-free survival and risk of distant metastasis in rare and prognostically poor tumors, such as uveal melanoma (UM) [10–15] and malignant mesothelioma (MM) [16–19].

4. Future Perspectives

The introduction of new molecular tests, including fluorescence in situ hybridization (FISH), real-time polymerase chain reaction (rt-PCR) or next generation sequencing (NGS) has not replaced IHC, that, due to its low costs and its immediate applicability, remains the most used first level test [3]. The 11 published papers included within this Special Issue provide the scientific community with new potential application fields of IHC in human neoplastic and non-neoplastic diseases, emphasizing the concept that the identification of new factors capable of predicting the biological behavior of diseases must represent a direction to follow in medical scientific research.

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References

1. Sukswai, N.; Khoury, J.D. Immunohistochemistry Innovations for Diagnosis and Tissue-Based Biomarker Detection. *Curr. Hematol. Malig. Rep.* **2019**, *14*, 368–375. [CrossRef] [PubMed]
2. Coons, A.H.; Creech, H.J.; Jones, R.N. Immunological properties of an antibody containing a fluorescent group. *Proc. Soc. Exp. Biol. Med.* **1941**, *47*, 200–202. [CrossRef]
3. Broggi, G.; Salvatorelli, L. Bio-Pathological Markers in the Diagnosis and Therapy of Cancer. *Cancers* **2020**, *12*, 3113. [CrossRef] [PubMed]
4. Castorina, S.; Lombardo, C.; Castrogiovanni, P.; Musumeci, G.; Barbato, E.; Almeida, L.E.; Leonardi, R. P53 and VEGF expression in human temporomandibular joint discs with internal derangement correlate with degeneration. *J. Biol. Regul. Homeost. Agents* **2019**, *33*, 1657–1662. [CrossRef] [PubMed]
5. Loreto, C.; Lombardo, C.; Caltabiano, R.; Filetti, V.; Vitale, E.; Seminara, D.; Castorina, S.; Fenga, C.; Ledda, C.; Rapisarda, V. Immunohistochemical expression and localization of MMP-9, MMP-13, E-Cadherin and Ki-67 in road pavers' skin chronically exposed to bitumen products. *Histol. Histopathol.* **2019**, *34*, 1141–1150. [CrossRef] [PubMed]
6. Magro, G.; Salvatorelli, L.; Puzzo, L.; Piombino, E.; Bartoloni, G.; Broggi, G.; Vecchio, G.M. Practical approach to diagnosis of bland-looking spindle cell lesions of the breast. *Pathologica* **2019**, *111*, 344–360. [CrossRef] [PubMed]
7. Certo, F.; Altieri, R.; Maione, M.; Schonauer, C.; Sortino, G.; Fiumanò, G.; Tirrò, E.; Massimino, M.; Broggi, G.; Vigneri, P.; et al. FLAIRectomy in Supramarginal Resection of Glioblastoma Correlates with Clinical Outcome and Survival Analysis: A Prospective, Single Institution, Case Series. *Oper. Neurosurg.* **2020**, opaa293. [CrossRef] [PubMed]
8. Cammarata, F.P.; Forte, G.I.; Broggi, G.; Bravatà, V.; Minafra, L.; Pisciotta, P.; Calvaruso, M.; Tringali, R.; Tomasello, B.; Torrisi, F.; et al. Molecular Investigation on a Triple Negative Breast Cancer Xenograft Model Exposed to Proton Beams. *Int. J. Mol. Sci.* **2020**, *21*, 6337. [CrossRef] [PubMed]
9. Broggi, G.; Filetti, V.; Ieni, A.; Rapisarda, V.; Ledda, C.; Vitale, E.; Varricchio, S.; Russo, D.; Lombardo, C.; Tuccari, G.; et al. MacroH2A1 Immunoexpression in Breast Cancer. *Front. Oncol.* **2020**, *10*, 1519. [CrossRef] [PubMed]
10. Caltabiano, R.; Puzzo, L.; Barresi, V.; Ieni, A.; Loreto, C.; Musumeci, G.; Castrogiovanni, P.; Ragusa, M.; Foti, P.; Russo, A.; et al. ADAM 10 expression in primary uveal melanoma as prognostic factor for risk of metastasis. *Pathol. Res. Pract.* **2016**, *212*, 980–987. [CrossRef] [PubMed]
11. Salvatorelli, L.; Puzzo, L.; Bartoloni, G.; Palmucci, S.; Longo, A.; Russo, A.; Reibaldi, M.; Vinciguerra, M.; Li Volti, G.; Caltabiano, R. Immunoexpression of Macroh2a in Uveal Melanoma. *Appl. Sci.* **2019**, *9*, 3244. [CrossRef]
12. Broggi, G.; Musumeci, G.; Puzzo, L.; Russo, A.; Reibaldi, M.; Ragusa, M.; Longo, A.; Caltabiano, R. Immunohistochemical Expression of ABCB5 as a Potential Prognostic Factor in Uveal Melanoma. *Appl. Sci.* **2019**, *9*, 1316. [CrossRef]
13. Russo, D.; Di Crescenzo, R.M.; Broggi, G.; Merolla, F.; Martino, F.; Varricchio, S.; Ilardi, G.; Borzillo, A.; Carandente, R.; Pignatiello, S.; et al. Expression of P16INK4a in Uveal Melanoma: New Perspectives. *Front. Oncol.* **2020**, *10*, 562074. [CrossRef]
14. Broggi, G.; Russo, A.; Reibaldi, M.; Russo, D.; Varricchio, S.; Bonfiglio, V.; Spatola, C.; Barbagallo, C.; Foti, P.V.; Avitabile, T.; et al. Histopathology and Genetic Biomarkers of Choroidal Melanoma. *Appl. Sci.* **2020**, *10*, 8081. [CrossRef]

15. Broggi, G.; Ieni, A.; Russo, D.; Varricchio, S.; Puzzo, L.; Russo, A.; Reibaldi, M.; Longo, A.; Tuccari, G.; Staibano, S.; et al. The Macro-Autophagy-Related Protein Beclin-1 Immunohistochemical Expression Correlates with Tumor Cell Type and Clinical Behavior of Uveal Melanoma. *Front. Oncol.* **2020**, *10*, 589849. [CrossRef] [PubMed]
16. Loreto, C.; Ledda, C.; Tumino, R.; Lombardo, C.; Vitale, E.; Filetti, V.; Caltabiano, R.; Rapisarda, V. Activation of caspase-3 in malignant mesothelioma induced by asbestiform fiber: An in vivo study. *J. Biol. Regul. Homeost. Agents.* **2020**, *34*, 1163–1166. [CrossRef] [PubMed]
17. Filetti, V.; Vitale, E.; Broggi, G.; Hagnäs, M.P.; Candido, S.; Spina, A.; Lombardo, C. Update of in vitro, in vivo and ex vivo fluoro-edenite effects on malignant mesothelioma: A systematic review (Review). *Biomed. Rep.* **2020**, *13*, 60. [CrossRef] [PubMed]
18. Loreto, C.; Caltabiano, R.; Graziano, A.C.E.; Castorina, S.; Lombardo, C.; Filetti, V.; Vitale, E.; Rapisarda, G.; Cardile, V.; Ledda, C.; et al. Defense and protection mechanisms in lung exposed to asbestiform fiber: The role of macrophage migration inhibitory factor and heme oxygenase-1. *Eur. J. Histochem.* **2020**, *64*, 3073. [CrossRef] [PubMed]
19. Loreto, C.; Lombardo, C.; Caltabiano, R.; Ledda, C.; Hagnas, M.; Filetti, V.; Rapisarda, V. An in vivo immunohistochemical study on MacroH2A.1 in lung and lymph-node tissues exposed to an asbestiform fiber. *Curr. Mol. Med.* **2020**, *20*. [CrossRef] [PubMed]