Melanoma is a serious type of skin cancer that begins in melanocytes, cells responsible for melanin production. It is one of the most aggressive forms of skin cancer due to its potential to spread to other parts of the body if not detected and treated early. Melanoma is caused by a combination of environmental (excessive exposure to ultraviolet radiation) and genetic factors. The most common mutation in melanoma patients is the missense mutation V600E in B-Raf murine sarcoma viral oncogene homolog B (BRAF), which triggers constitutive activation of the RAS/RAF/MEK/ERK (hereafter MAPK) signaling pathway, that results in enhanced proliferation and melanoma cell survival. Melanoma treatment depends on several factors including cancer stage, tumor location, and the presence of genetic mutations. The development of targeted therapies employing specific and selective BRAF-mutated kinase inhibitors (vemurafenib, dabrafenib and encorafenib) used alone or in combination with MEK kinase inhibitors (trametinib, cobimetinib and binimetinib) revolutionized the therapy of melanoma patients, however, the initial response to treatment is often followed by drug resistance and melanoma recurrence. Therapy resistance in melanoma could be driven by genetic changes leading to the reactivation of the MAPK pathway, activation of alternative signaling pathways, and adaptive cell plasticity leading to phenotype switching. The mechanisms of acquired drug resistance in melanoma cells are complex, and despite extensive research are still not fully understood, therefore, a better understanding of the molecular landscape of melanoma is necessary to propose novel targets or target combinations for selective therapeutic intervention

β-catenin is a multifunctional protein that can either bind to cadherin which is an integral part of the actin cytoskeleton, or act as a transcriptional coactivator. It is the central component of the canonical WNT signaling pathway that mainly controls important cellular processes throughout embryonic development and adult tissue homeostasis, therefore deregulation of WNT-signaling contributes to cancer initiation, progression and modulation of the immune microenvironment. Moreover, recent studies have highlighted the crosstalk between the MAPK and WNT/β-catenin pathways in melanoma and the aberrant activation of WNT/β-catenin signaling has been implicated in resistance development. Melanoma was one of the first tumors associated with β-catenin dysregulation, however, its role in melanoma biology remains not fully elucidated and is highly controversial to date despite extensive studies [Gajos-Michniewicz A. i wsp. 2020]. As the role in melanoma biology remains not fully understood, my scientific interests are concentrated on investigating WNT/β-catenin signaling in drug-naïve and drug-resistant melanoma cells. According to preliminary studies carried out in the MINIATURA-5 project, financed by the National Science Centre, drug-naïve and drug-resistant melanoma cells differ in the basic activity of the canonical WNT signaling pathway and their response toward WNT/β-catenin signaling inhibitor is also differential. Therefore, the potential of research on the role of the WNT/β-catenin pathway in the progression and development of melanoma drug resistance is high and the modulation of the activity of this pathway may be treated as a novel therapeutic approach in the future.

Gajos-Michniewicz A, Czyz M. WNT Signaling in Melanoma. Int J Mol Sci. 2020, 21(14):4852.