

Current Topics on Cancer Stem Cell Associated Melanoma Treatment Researches

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Melanoma Treatment

Malignant tumor of melanocytes describes as “melanoma”. Melanocytes are derived from the neural crest and make the pigment melanin [1]. Despite most melanomas emerge in the skin, they may arise on mucosal surfaces or eyes and rarely intestines. A common point of these organs is the migration of neural crest cells [2,3]. An expected 13.7 million Americans with cancer background were alive on 2012. In the same report, in 2022, it is expected that number will increase approximately 18 million. It makes melanoma the 3rd most prevalent cancers among males [4]. The risk factors are environmental factors, family history, characteristics of pigment, multiple nevi, immunosuppression and genetic factors [5,6].

We should understand the importance of the relation between cancer stem cells and genetic regulations to develop a therapy. Stem cells are defined as cells that have the ability to immortalize themselves through self-renewal and to differentiate to mature cell of significant tissue. However, there are also cancer stem cells within definite proliferative potential and ability to growth tumors [7]. Rare stem cells which may cause cancer are related with genes. Most importantly, most frequent mutations in cutaneous melanoma appear in BRAF (V-raf murine sarcoma viral oncogene homolog B1) genes [8]. Nearly, up to 60% of malignant melanomas generates from a single transition in BRAF [9]. Lessly NRAS (neuroblastoma RAS viral [v-ras] oncogene homolog), c-KIT, CDK4 are responsible, too [10,11].

Researches are focused on four main topics: transcriptional response, tumor microenvironment, marker and pathways [12-15]. Following novel ones chosen to represent each topic.

Chen et al. turned their way to nature. They suggested that a licorice extract: Isoliquiritigenin (ISL) may cause B16F0 melanoma cell differentiation. Here, researchers investigated the differentiation process of the transcriptional response of ISL-inducing. They searched for 390 genes which have roles in 201 biochemical pathways and found out altered expression levels in ISL treatment. Different expression of anti-proliferative and differentiation inducing genes indicated malignancy loss [12].

Findings of studies suggest that Ipilimumab plus bevacizumab therapy supports immunity in the tumor microenvironment via enhanced lymphocyte infiltration and antibody responses [13,14]. IL1 alpha, TNF-alpha, and CXCL10, with VEGF neutralization, contribute to ipilimumab plus bevacizumab-induced melanoma immune recognition [15]. CD271 is a neurotrophin receptor. It expresses in

melanoma. Saltari et al. investigated CD271 characteristics extensively. They found following results in zebrafish in vitro: CD271 overexpression in SKMEL28 cells reduced invasion, CD271 overexpressing 1205Lu cells was in a relationship with fewer metastases percentage, the absence of CD271 caused reduced cell-cell adhesion. All of them indicate that loss of CD271 is crucial for melanoma metastasis and progression [16]. Surveys showed that CD271-positive melanoma stem cells showed correlations with metastasis, not prognosis in humans. These cells are multipotent and can create heterogeneity tumor after maturity In vivo they have self-renewal capacity and maintain tumor growth [17,18].

Notch and ERBB are essential for melanocyte precursors. In their study Zhang et al. show that in mutated and wild-type BRAF melanomas; active Notch1 and active ERBB3, ERBB2 correlates and expression levels are similar [19]. Blocking Notch and ERBB signaling at the same time, inhibits the slow cycling of JARID1B+ cell population. Due to JARID1B+ cells represent cancer stem cells, this is crucial for melanoma growth continuation in long term [20]. Kaushik et al. also reported that Notch2 pathway is effective on melanoma. As a result, these results propose regulating these pathways is an advance way for melanoma treatment [19].

Today, there are more researches on the pathway, tumor microenvironment, and marker. The information obtained from these studies may lead to the emergence of new treatment strategies and activities of therapeutic agents. These research examples are the pioneers, and potentially have high impact.

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