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Susceptibility of craniofacial ciliopathies to oral cancer-A proposed research

Abstract

The Ciliary disorders are a group of clinically and genetically overlapping disorders, manifesting as syndromes, whose patho-physiology arises due to defective ciliary function including its organelles. These are antenna-like organelles are present in the apical surface of numerous cell types in a variety of tissues and organs, in humans, currently under research in medico genetic field.[1] During organogenesis, although the neural crest receives a significant amount of attention, craniofacial tissue has more patterning information present when compared to other tissues of the body.[2] Newer studies have further indicated the importance of ciliary epithelia as a source of patterning information for the tissues in orofacial region. In this article, we propose a research in patients with craniofacial ciliopathies linking to origin of cancers in oro-facial region.

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Introduction

The current research on the primary cilium, which is an organelle that coordinates and transduces signals in the molecular environment in various tissues of the human body has lead the way in a fresh view for understanding the etio pathogenesis of many craniofacial disorders[3] including oral cancer, which is the sixth most common cancer in the world among various groups of population. If an individual gets exposed to environmental agents and the byproducts of their cellular metabolism, resulting in damage to DNA including genes, which are susceptible to cancer is called as genetic polymorphism.[4] The genetic basis of risk of cancer in craniofacial region has been enhanced most recently by establishment of genotype-phenotype correlations in human beings and identification of various factors, including genetic and environmental, which may modify the risk.[5]

Research prospects in ciliopathies

The Primary cilia are the organelles that mediate intercellular signaling pathways which are involved in the regulation of cellular process resulting in the formation and maintenance of all organs and vital structures inside the human body during organogenesis. The term cancer is defined as "uncontrolled cell division as well as an impaired ability to undergo apoptosis[6] and develops as a result of altered intra and intercellular signaling, including the disturbances of ciliary mediated signaling pathways may result in formation of tumors.[7–9] The studies have shown that WNT signaling is restricted by cilia. Also a few publications have shown cilia-dependent mediation of sonic hedgehog signaling (SHH), transforming growth factor (TGF-β), platelet-derived growth factor receptor-α (PDGFR-α), WNT signaling (non-canonical), cilia-regulated proteasome and other altered cell-signaling process.[10]

The understanding of hereditary basis of the craniofacial ciliopathies to cancers in orofacial region may lead to identification of new molecular markers for treating the disease through novel therapeutic targets.[11] The phenotypes of ciliopathies affecting the orofacial region ranges from most understood oro-facial digital syndrome [by Franco et al][12] to less common and life-threatening embryonal tumor with multilayered rosettes. Citing a few researches made in cancers occurring in other sub-types, WD 40-Repeat Proteins in ciliopathies have shown cancer-associated PALB2 mutations cause the loss of its binding ability to BRCA2/RAD51C and biallelic mutations of PALB2 are associated with increased occurrence of childhood cancers.[13] FBXW7 is an ubiquitin ligase substrate receptor and most commonly deregulated ubiquitin proteasome system protein in human cancer.[14] The loss-of-function mutations in FBXW7 may result in inappropriate accumulation of cyclin E. These mutations are observed in 18% of colorectal cancers, 15% of uterine endometrial carcinoma and 40% of patients with uterine carcinosarcoma.[15]

The research made in relation to prevalence of risk factors in patients with craniofacial ciliopathies to cause oral cancer is yet to be published, for the clinicians to deepen the knowledge of these ciliopathies. This will help the physicians to recognize the type of disability afflicting the patient and offer optimum inter-disciplinary treatment to improve the overall lifestyle of the affected patients.

Conclusion

The future research in finding the associated mutations in ciliary disorders will significantly contribute significantly to the health care burden and will revolutionize the treatment approach to the patients with risk of cancers in orofacial region associated with ciliary disorders. It will also provide a bridge between gene specialists and clinicians to understand the complex clinical manifestations of cilopathies.

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Conflicts of interest

The author declares no conflicts of interest.

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