Cartilage Oligomeric Matrix Protein and Colorectal Cancer

Kyle Becnel[1], Mohammad Afaque Alam[2], Valentine N. Nfonsam[2]
[1]Louisiana State University Health Sciences Center School of Medicine, New Orleans, LA 70112
[2]Louisiana State University Health Sciences Center Department of Surgery, New Orleans, LA 70112

Introduction

- **Colorectal cancer (CRC) is the third most diagnosed cancer in the United States and the second most common cause of cancer-related death in males under age 50.[1]**
- **While the total incidence of CRC has decreased since 1985 by 46%, incidence in patients under the age of 50, or early-onset (EOCRC), has increased.[1]**
- **EOCRC, which more typically arises in the left colon and exhibits signet-ring morphology with a mucinous and poorly differentiated appearance on histological examination, is molecularly and histopathologically distinct from late-onset CRC.[2,3,4]**
- **Cartilage oligomeric matrix protein (COMP) expression was shown to be significantly elevated in EOCRC cells, implicating a potential role in the development of the cancer.[3]**
- **COMP is expressed in several tissue types, playing a key role in the assembly and stabilization of the extracellular matrix.[5,6]**
- **Elevated serum levels are correlated with several pathologies, including pseudoachrondroplasia, multiple epiphyseal dysplasia, osteoarthritis, cardiovascular disease, and a growing number of cancers. These include hepatocellular, ovarian, prostate, breast, and colorectal cancers.[7]**
- **In cancer, elevated serum COMP levels are correlated with higher recurrence rate of malignancy, poorer survival rates, and the stage and grade of the cancer.[8,9]**
- **Recent studies have aimed to elucidate the specific signaling pathways COMP utilizes in the progression of various cancers, including CRC and EOCRC.[10] This review aimed to summarize the current understanding of the role COMP plays in the progression of CRC and identify areas for further investigation.**

COMP and Cellular Proliferation

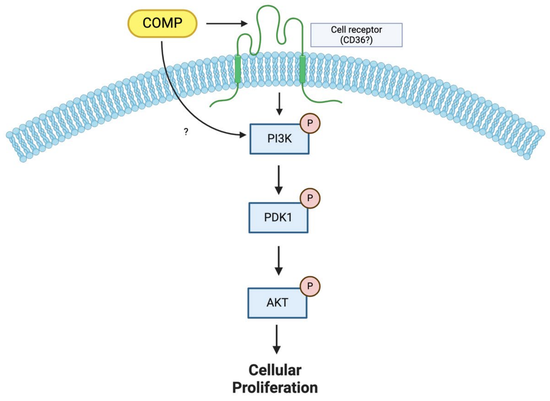

Figure 1: Overexpression of COMP leads to hyperactivity of the PI3K/Akt pathway, promoting cellular proliferation.[11]

COMP and Apoptosis

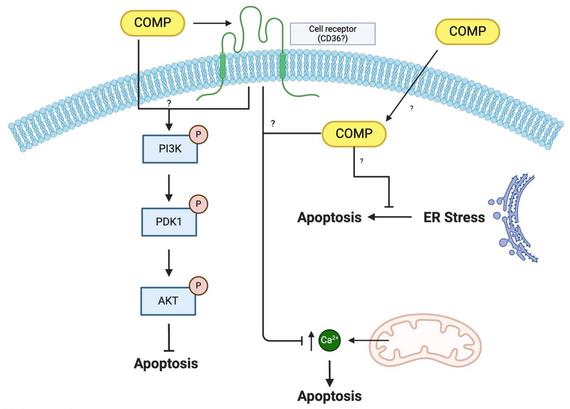

Figure 2: COMP overexpression aids in the evasion of apoptosis, but the exact mechanism in CRC is unclear.[12,13,14]

COMP and the EMT

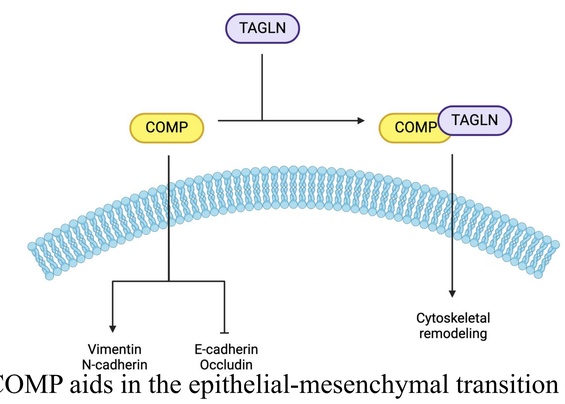

Figure 3: COMP aids in the epithelial-mesenchymal transition (EMT) by promoting the expression of mesenchymal markers and cytoskeletal remodeling in association with TAGLN.[13]

COMP and Immune Response

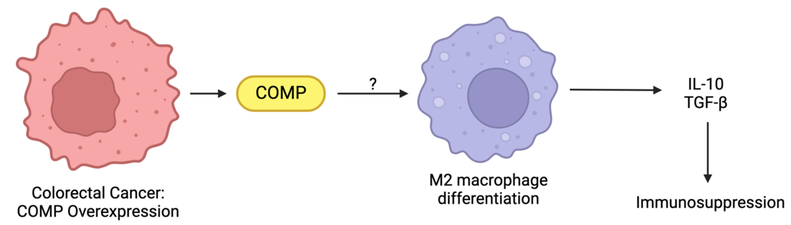

Figure 4: COMP overexpression induces macrophages to differentiate into the M2 phenotype, which then releases immunosuppressive cytokines.[14]

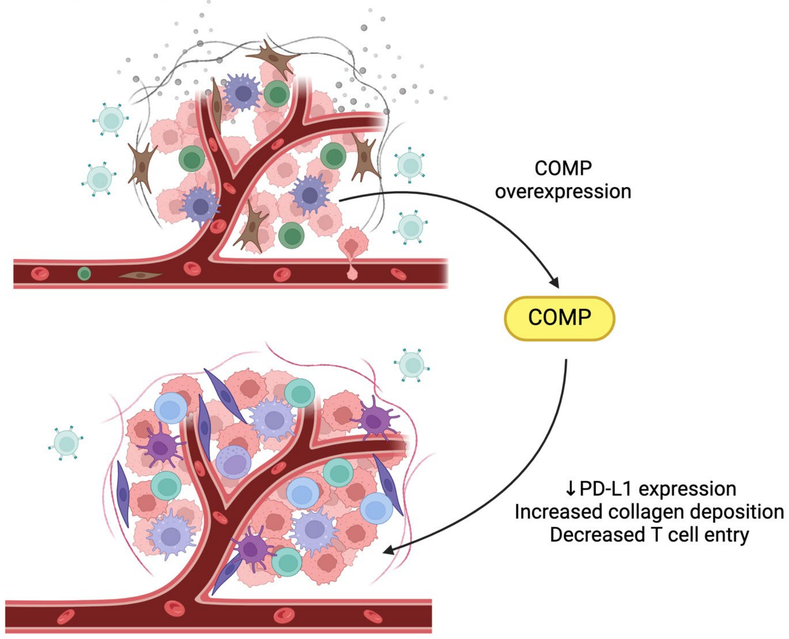

Figure 5: COMP overexpression results in a decrease in PD-L1 expression, increased collagen deposition by the cancer-associated fibroblasts (CAFs), and decreased T cell entry into the tumor microenvironment (TME).[15]

Conclusion

- **CRC continues to be a significant concern for patient morbidity and mortality. Serum COMP levels are correlated with the progression of EOCRC, implicating its role in the disease.**
- **COMP promotes cellular proliferation, aids in evading apoptosis and the immune system, and promotes the epithelial-mesenchymal transition.**
- **Future studies should clarify the exact mechanisms by which CRC aids in the evasion of apoptosis and promotes M2 macrophage differentiation and its effects on tumor metabolism and ER function.**

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