Conclusion

Aberrant Wnt activation induced CIN and MMR inactivation induced MSI may account for a majority of aging related colon cancer; the predominant CRC subtype in the Western world. Several therapeutic approaches targeting the Wnt pathway are being tested and are expected to improve survival in metastatic late-onset colon cancer. However, as discussed above, it may not be accurate to assume a significant role of CIN and MMR inactivation in all forms of CRC. CRC in the developing world is predominantly a disease of the rectum occurring at a younger age. The current study revealed absence of the two main CRC pathways in a significant proportion of early onset CRC, especially in RC. In the absence of the two pathways, our study has identified the presence of non-canonical Wnt pathway, yet unable to suggest whether the same is involved in the genesis of the tumor or as a genetic event occurring during the multistep progression of CRC. Further studies using Immunohistochemistry on a larger independent sample set and primary tumor tissue culture are required to identify the extent and role of non-canonical Wnt signaling in CRC in Indian genetic background. Our novel findings therefore include identification of a substantial proportion of early onset patients not harboring either CIN or MSI, which may have therapeutic implication. The role of non-canonical Wnt signaling in early onset CRC has not been investigated before. It is hoped that our study may lead to potential drug targets in early onset CRC in the Indian genetic background. Given that the worldwide CRC burden is becoming prominent in developing nations where the molecular and clinico-pathological CRC profile appears to be distinctly different, it is imperative to
understand CRC biology in early-onset RC. Ongoing research in several laboratories is expected to hasten novel discoveries in the field of CRC molecular origin; which holds the promise for better patient management and treatment options for CRC in the developing world not driven by Wnt or MSI.