

Early Onset Colorectal Cancer Executive Briefing

Early Onset Colorectal Cancer Group MD Anderson Cancer Center (MDACC)

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Background & Summary:

The incidence of early-onset colorectal cancer (EOCRC) has been alarmingly increasing in people less than 50 years old to more than 50% since 1994 (1). EOCRC is defined as colon and rectal cancers diagnosed before the age of 50 years old. The number of diagnosed EOCRC cases is expected to increase to over 140% by 2030 (2). The raising of EOCRC made it the second most common cancer and the third cause of cancer mortality for this age group (1,3). Although the mortality rate of late-onset CRC in people aged 50 or older (LOCRC) declined by around 34%, it has raised in EOCRC by 13% (3). This trend of increased incidence of EOCRC is observed internationally as well (4). Clinically, over 70% of EOCRC patients are diagnosed at stage III or IV with a delay in diagnosis of at least six months in around 40% of cases.

While around 30% of EOCRC cases are hereditary; the remaining 70% of driver mutations are unknown (5). In addition, EOCRC has different signatures than LOCRC that has not been catalogue in detail yet (6). Exposome is the human environmental exposures of external or internal environmental risk factors such as antibiotic or gut microbiota. Exposome has been linked to EOCRC in epidemiological studies. However, more concrete studies are needed to evaluate the role of exposome in the biological mechanism and development of EOCRC (7).

Recommended Reading:

1. Early-onset colorectal cancer: initial clues and current views (7).
2. Clinical and molecular characterization of early-onset colorectal cancer (6). * MDACC
3. Cumulative Burden of Colorectal Cancer–Associated Genetic Variants Is More Strongly Associated With Early-Onset vs Late-Onset Cancer (8).
4. Epidemiology and Mechanisms of the Increasing Incidence of Colon and Rectal Cancers in Young Adults (9).
5. Trends in Incidence of Early-Onset Colorectal Cancer in the United States Among Those Approaching Screening Age (10).
6. Colon Cancer in Patients Under 25 Years Old: A Different Disease? (11) * MDACC
7. Risk Factors for Early-Onset Colorectal Cancer (12).
8. Clinical and molecular characterization of early-onset colorectal cancer patients with inflammatory bowel disease (13). * MDACC
9. Early warning a decade ago about the rising trends of early onset CRC (14). * MDACC

Links to recommended talks from NIH Early Onset Colorectal Cancer Think Tank, 2020:

1. What is known about incidence and mortality trends, birth cohort effects, and associations with risk factors?: **Rebecca Siegel**
(<https://mdacc.box.com/s/9wpfmlag93jzd2va88h9x30egeml05wj>)
2. Etiological factors of EO-CRC: **Rick Woychik**.
(<https://mdacc.box.com/s/ssiwra6vklku9l9d1rme42bwdgyn0xxo>)
3. Translational opportunities and clinical experiences: **John Carpten**.
(<https://mdacc.box.com/s/2mpawn4spimjyk45sakd61lu0gplu1pj>)
4. Pathology of disease: **Lisa Boardman**.
(<https://mdacc.box.com/s/07tq4q76jxicgy289qvczstg8b49xk9q>)
5. Critical gene-environment interactions: **C. Richard Boland**.
(<https://mdacc.box.com/s/8et8qojvhd0got87a12ibhsum2njln0r>)
6. Molecular biological features of EO-CRC: **David Shibata**.
(<https://mdacc.box.com/s/sd57mnueb5jjj5vp65jb6ptfepgiq369>)
7. Biological mechanisms of EO-CRC: **Kimmie Ng**.
(<https://mdacc.box.com/s/6ets8nn5sboyf13wkk1hma5j31ubx44t>)
8. Lack of APC somatic mutations in EO-CRC in African Americans: **Nathan A. Ellis**.
(<https://mdacc.box.com/s/pmrns5ga8d2o1n3wjq7nwgy6py0yq12t>)
9. Molecular aspects of EO-CRC: **Scott Kopetz**.
(<https://mdacc.box.com/s/zo4qknnx84hoo4rr8zg91e7u6udqy940>)
10. Potential risk factors, including diet and microbiota: **Andrew T. Chan**.
(<https://mdacc.box.com/s/1qnv520yilf9e39vpuyetng59v4rmgh9>)
11. Earlier life exposures: maternal obesity and gestational growth: **Caitlin Murphy**.
(<https://mdacc.box.com/s/dmfqed5y6vp2x9cav1twe3e1q413cubf>)
12. Microbiome interactions: **Cynthia L. Sears**
(<https://mdacc.box.com/s/wbwr45hg71gk7c9lj2d9okv44w2q35ke>)
13. Dietary and environmental exposures: **Stephen Baylin**
(<https://mdacc.box.com/s/6z5rtjsd2o1a4yrofumib1j2bgl6hs57>)

References:

1. Siegel RL, Miller KD, Goding Sauer A, Fedewa SA, Butterly LF, Anderson JC, et al. Colorectal cancer statistics, 2020. *CA Cancer J Clin* [Internet]. 2020 Mar 5; Available from: <http://dx.doi.org/10.3322/caac.21601>
2. Bailey CE, Hu C-Y, You YN, Bednarski BK, Rodriguez-Bigas MA, Skibber JM, et al. Increasing disparities in the age-related incidences of colon and rectal cancers in the United States, 1975-2010. *JAMA Surg*. 2015 Jan;150(1):17-22.
3. Patel SG, Ahnen DJ. Colorectal Cancer in the Young [Internet]. Vol. 20, *Current Gastroenterology Reports*. 2018. Available from: <http://dx.doi.org/10.1007/s11894-018-0618-9>

4. Siegel RL, Jakubowski CD, Fedewa SA, Davis A, Azad NS. Colorectal Cancer in the Young: Epidemiology, Prevention, Management. *Am Soc Clin Oncol Educ Book*. 2020 Mar;40:1–14.
5. Pearlman R, Frankel WL, Swanson B, Zhao W, Yilmaz A, Miller K, et al. Prevalence and Spectrum of Germline Cancer Susceptibility Gene Mutations Among Patients With Early-Onset Colorectal Cancer. *JAMA Oncol*. 2017 Apr 1;3(4):464–71.
6. Willauer AN, Liu Y, Pereira AAL, Lam M, Morris JS. Clinical and molecular characterization of early-onset colorectal cancer. *Cancer* [Internet]. 2019; Available from: https://onlinelibrary.wiley.com/doi/abs/10.1002/cncr.31994?casa_token=KiWnVC1Tpk0AAAAA:QpyFET0YWNyO9akYe4XsgqzkvKPHsLnW7bk-0VnO2CdWJMWyvLNP_9vj2eUQV0qh6MLNkr2GSJAKe8M
7. Hofseth LJ, Hebert JR, Chanda A, Chen H, Love BL, Pena MM, et al. Early-onset colorectal cancer: initial clues and current views. *Nat Rev Gastroenterol Hepatol*. 2020 Jun;17(6):352–64.
8. Archambault AN, Su Y-R, Jeon J, Thomas M, Lin Y, Conti DV, et al. Cumulative Burden of Colorectal Cancer-Associated Genetic Variants Is More Strongly Associated With Early-Onset vs Late-Onset Cancer. *Gastroenterology*. 2020 Apr;158(5):1274–86.e12.
9. Stoffel EM, Murphy CC. Epidemiology and Mechanisms of the Increasing Incidence of Colon and Rectal Cancers in Young Adults. *Gastroenterology*. 2020 Jan;158(2):341–53.
10. Abualkhair WH, Zhou M, Ahnen D, Yu Q, Wu X-C, Karlitz JJ. Trends in Incidence of Early-Onset Colorectal Cancer in the United States Among Those Approaching Screening Age. *JAMA Netw Open*. 2020 Jan 3;3(1):e1920407.
11. Hayes-Jordan AA, Sandler G, Malakorn S, Xiao L-C, Kopetz S, Rodriguez-Bigas M. Colon Cancer in Patients Under 25 Years Old: A Different Disease? [Internet]. Vol. 230, *Journal of the American College of Surgeons*. 2020. p. 648–56. Available from: <http://dx.doi.org/10.1016/j.jamcollsurg.2019.12.043>
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13. Willauer AN, Loree JM, Pereira AAL, Lam M, Raghav KPS, Morris VK, et al. Clinical and molecular characterization of early-onset colorectal cancer patients with inflammatory bowel disease [Internet]. Vol. 36, *Journal of Clinical Oncology*. 2018. p. 689–689. Available from: http://dx.doi.org/10.1200/jco.2018.36.4_suppl.689
14. You YN, Nancy You Y. Young-Onset Colorectal Cancer: Is It Time to Pay Attention? [Internet]. Vol. 172, *Archives of Internal Medicine*. 2012. p. 287. Available from: <http://dx.doi.org/10.1001/archinternmed.2011.602>