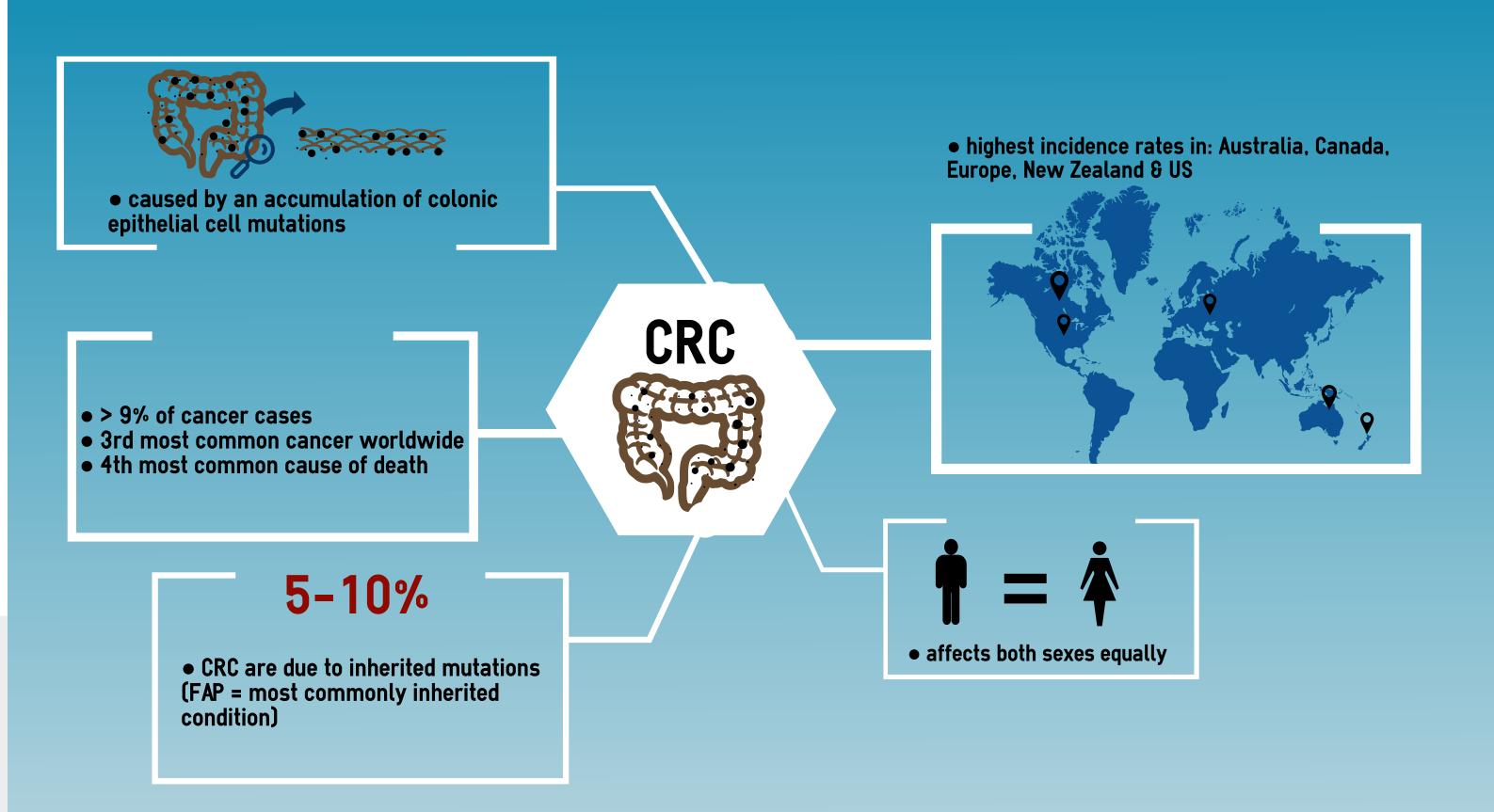
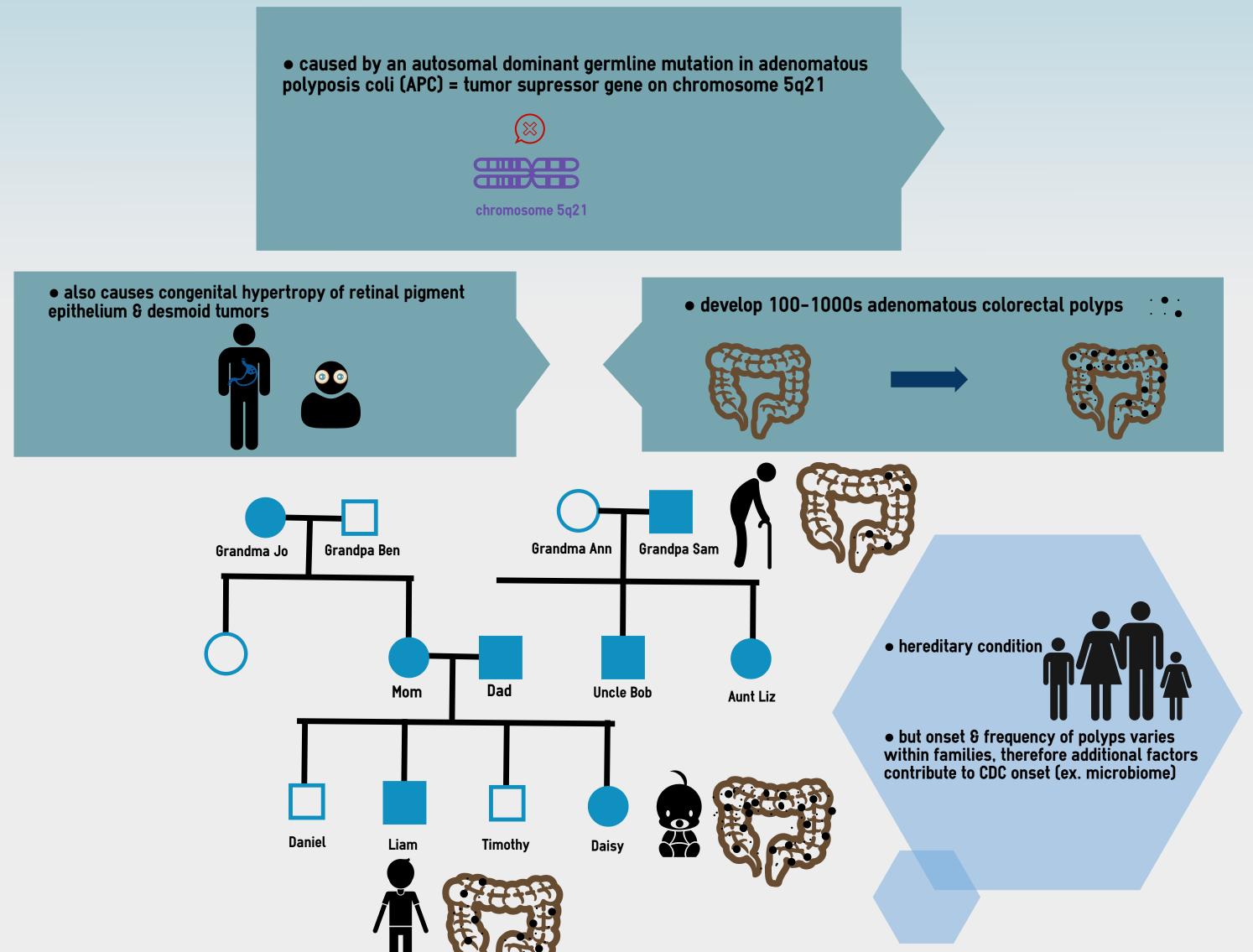


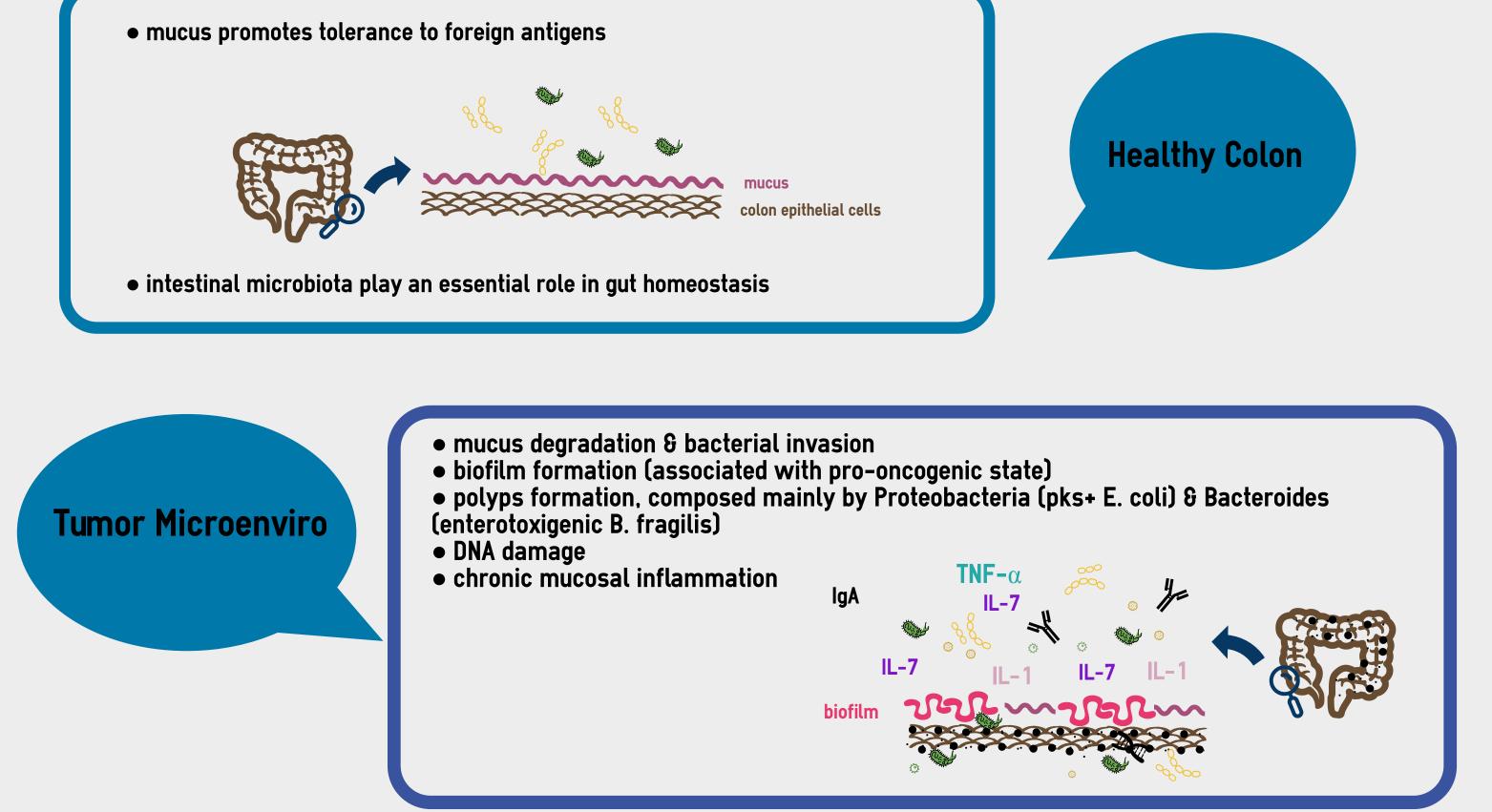
What is colorectal cancer (CRC)?



What is familial adenomatous polyposis (FAP)?

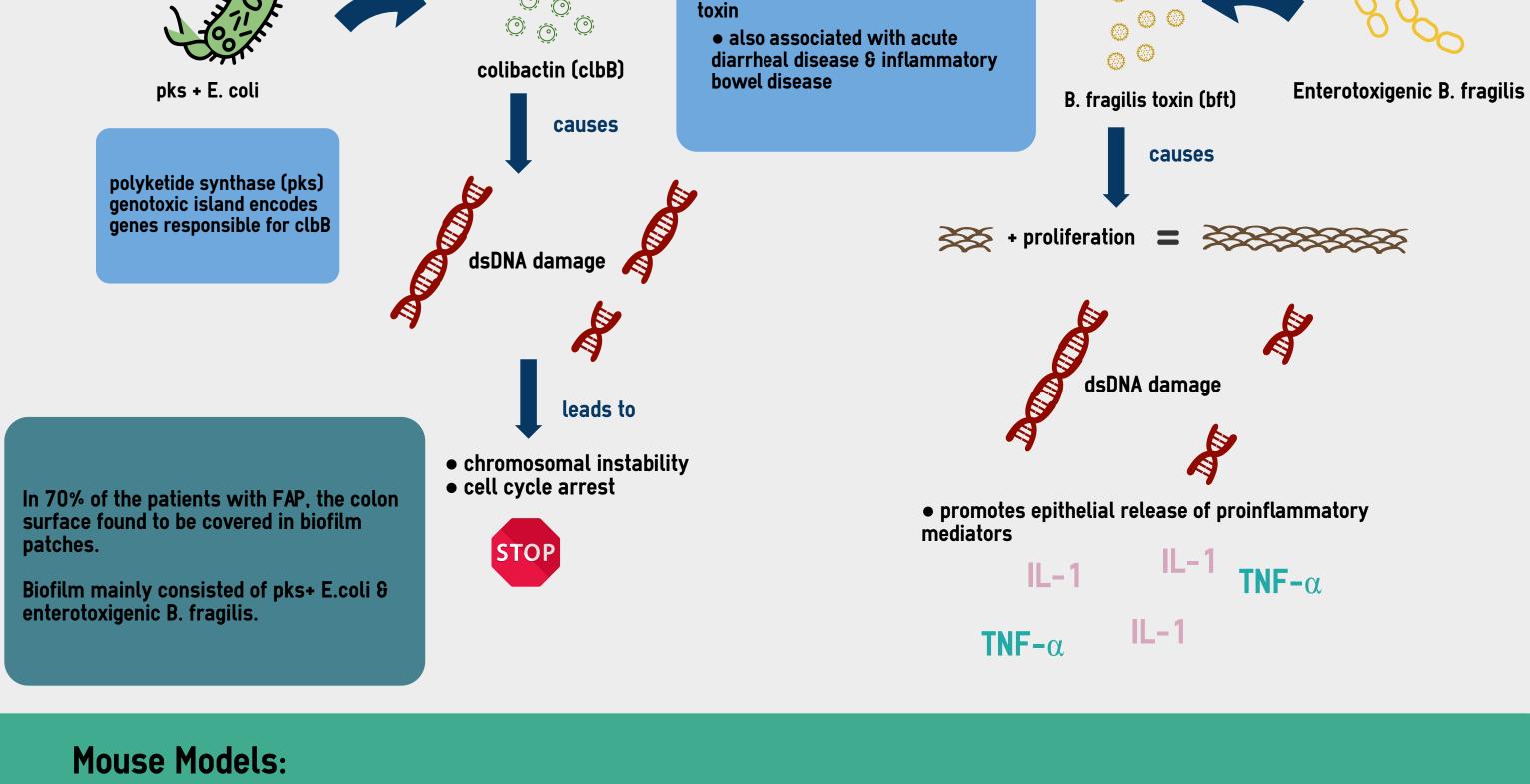


Healthy Colon vs. Tumor Microenvironment:

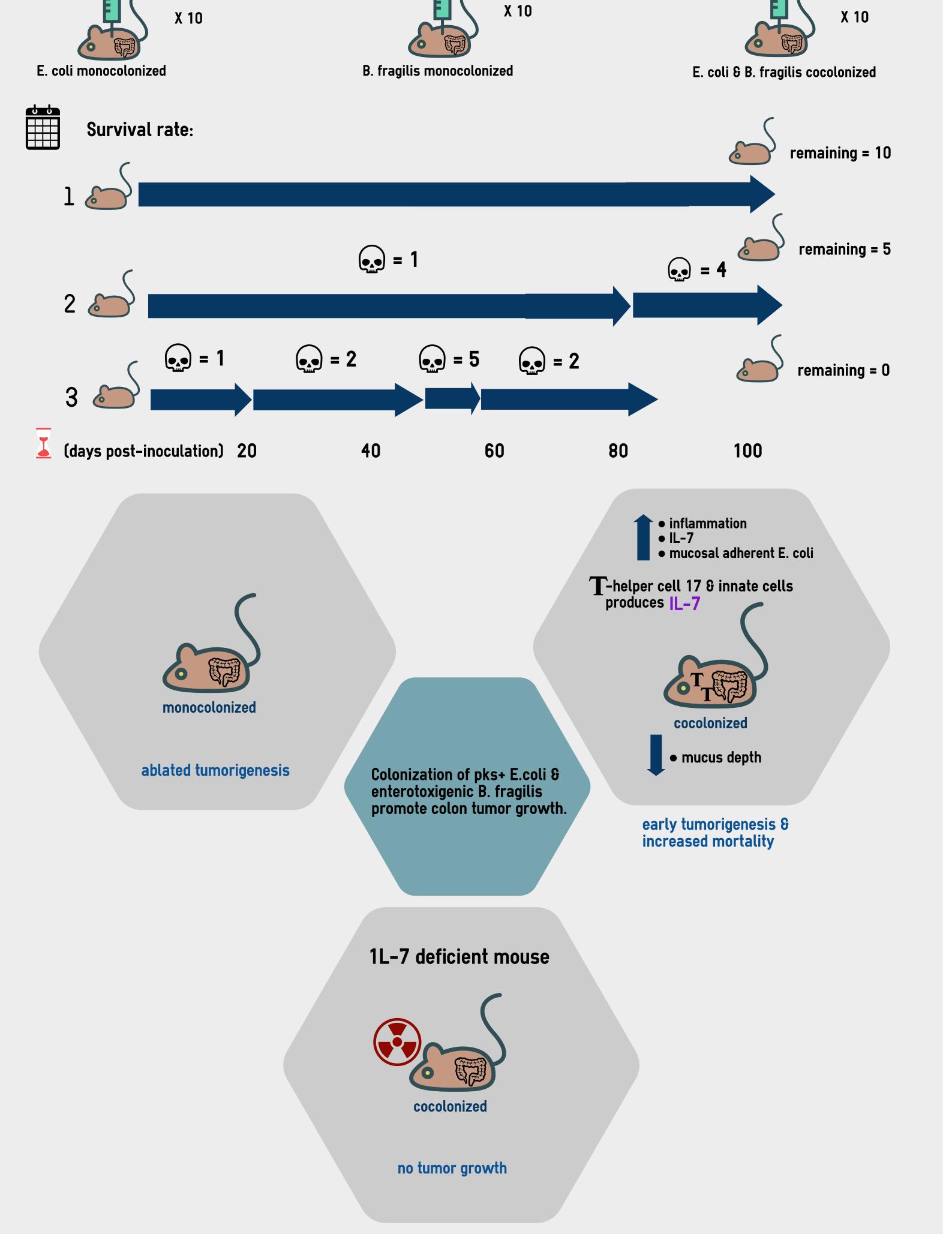


bft = zinc-dependent metalloprotease

Escherichia coli (E. coli) & Bacteroides fragilis (B. fragilis):



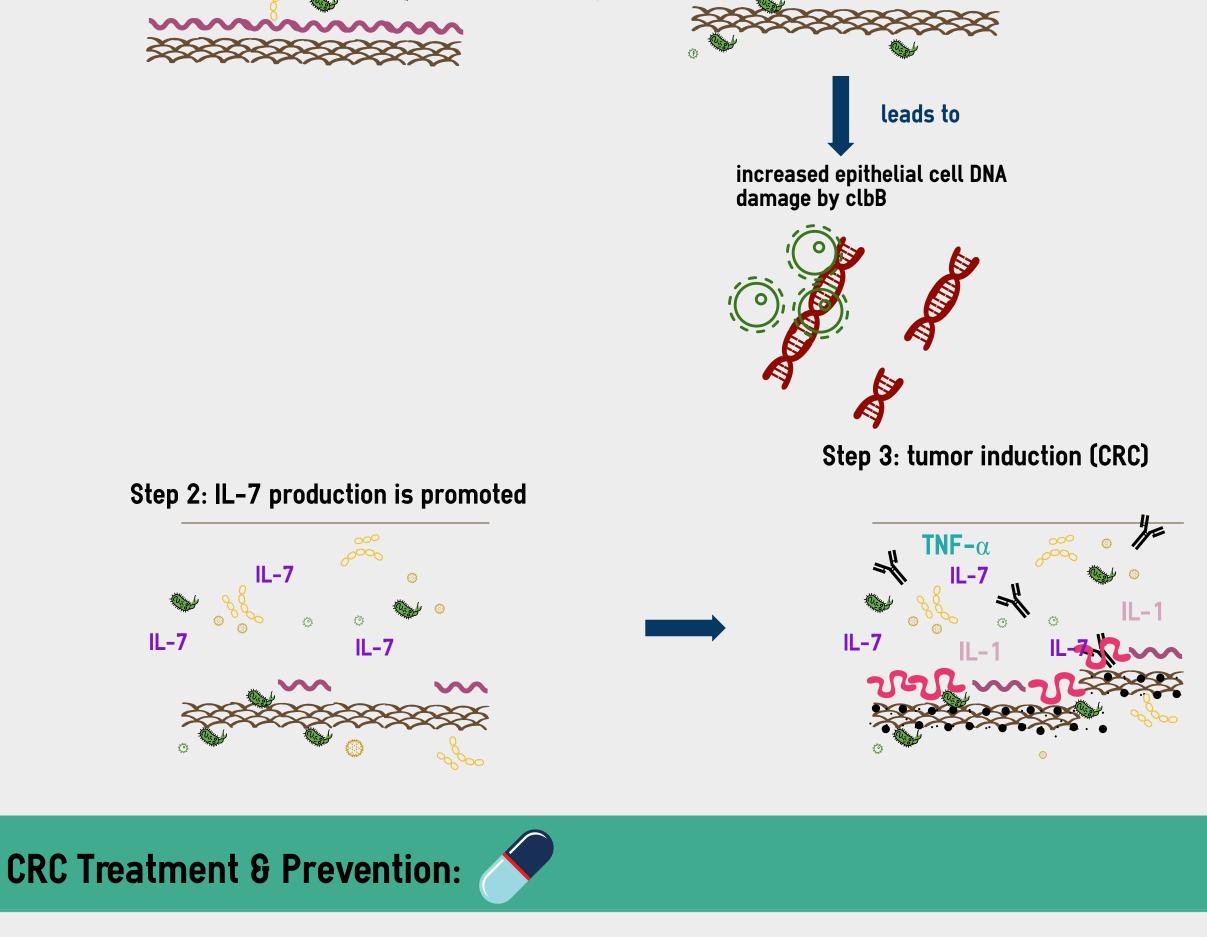
1



Mechanism?

increased epithelial cell DNA damage by clbB

Step 1: mucus degradation by enterotoxigenic B. fragilis allows increased E. coli adherence to colon epithelial cells



1. number 1 treatment: colectomy + chemotherapy

- 2. personalized anticancer chemotherapy treatment • adjuvant therapy targeting microbiota associated with carcinogensis • screening/detection for coexpression of bft & clbB
- clbB-inhibiting drugs • bft-inhibiting drugs (could also offer protection against acute diarrheal disease & inflammatory bowel disease) • prevention of mucus degradation by enterotoxigenic B. fragilis
- reduce IL-7 expression or activation

References:

Aoki, K. Taketo, M.M., Adenomatous polyposis coli (APC): a multi-functional tumor suppressor gene. J Cell Sci. 2007. 120: 3327-3335. Boleij, A., Hechenbleikner, E.M., Goodwin, A. C., Badani, R., Stein, E. M., Lazarev, M. G., Ellis, B., Carroll, K. C.,

Albesiano, E., Wick, E.C., Platz, E. A., Pardoll, E. M., Sears, C. L., The Bacteroides fragilis Toxin Gene Is Prevalent in the Colon Mucosa of Colorectal Cancer Patients. Clin Infect Dis. 2015. 60(2): 208-215. Dejea, C.M., Fathi, P., Craig, J.M., Boleij, A., Taddese, R., Geis, A.L., Wu, X., Shields, C. E. D., Hechenbleikner, E. M., Huso,

D. L., Anders, R. A., Giardiello, F. M., Wick, E. C., Wang, H., Wu, S., Pardoll, D. M., Housseau, F., Sears, C. L., Patients with familial adenomatous polyposis harbor colonic biofilms containing tumorigenic bacteria. Science. 2018. 359(6375): 592-597. Galiatsatos, P., Foulkes, W. D., Familial adenomatous polyposis. Am J Gastroenterol. 2006. 101(2):385-98.

Haggar, F. A., Boushey, R. P., Colorectal Cancer Epidemiology: Incidence, Mortality, Survival, and Risk Factors. Clin Colon Rectal Surg. 2009. 22(4): 191-197.

McCarthy, A. J., Martin, P., Cloup, E., Stabler, R. A., Oswald, E., Taylor, P. W., The Genotoxin Colibactin Is a Determinant of Virulence in Escherichia coli K1 Experimental Neonatal Systemic Infection. Infect. Immun. 2015. 83(9): 3704-3711.

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