Dear Editor of WJGO,

I am resubmitting MS 64748 "Can dietary flavonoids be useful in the treatment of colorectal cancer?", after introducing the changes suggested by the reviewer. I thank the helpful comments and the opportunity to improve the paper. Changes are marked in red in the text and correspond to additions and/or rearrangements to the text. A table and a figure were also added. A reply to the reviewer's comments is added to this letter.

I hope you find the MS acceptable for publication in WJGO.

Sincerely,

Cristina Pereira-Wilson

## Reply to reviewer's comments:

- With regard to addressing the role of phytochemicals in CRC pathogenesis, the published data is
  insufficient to establish this narrative. Relative to the strengths and weaknesses of the drugs
  available I emphasized in the text that downstream activating mutations in signaling pathways
  dependent on membrane receptors render cells resistant to current drugs and added a figure
  representative of the targets of CRC drugs and natural compounds.
- 2. Additional information was added in the form of a table as suggested with polyphenol subtypes and respective food sources.
- 3. About links between flavonoid classes and CRC subtypes I clarified in the text that the information available is inconclusive in this regard.
- 4. There are no toxicities associated with the amounts of flavonoids consumed as part of the foods in the regular healthy diet. Should they be used isolated and in pharmacological doses careful testing of toxicity needs to be carried out, also addressing possible drug-drug interaction effects. It is not a case of the more the better.
- 5. I have revised the referencing in the text in accordance with comments 5 and 6.
- 6. With regard to comment 7 I have added an abbreviation list.

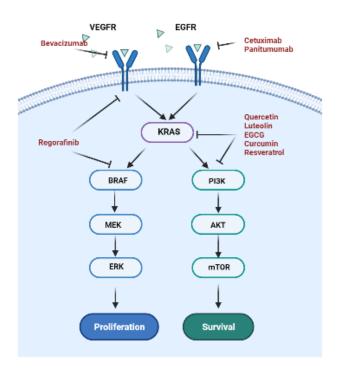


Figure 1

Table 1

Class of Polyphenol	Representative Compounds	Food Sources
Flavonol*	(+)-Catechin; (-)-Epicatechin Epigallocatechin gallate (EGCG)	Cocoa, Green Tea
Flavone*	Luteolin, Apigenin, Chrysin	Parsley, Red Peppers
Flavonol*	Quercetin, Rutin, Kaempferol	Onions, Broccoli, Apples
Flavanone*	Naringin, Naringenin, Hesperidin	Citrus fruits
Isoflavones*	Genistein, Daidzein	Soybean
Anthocyanidin*	Cyanidin, Delphinidin, Pelargonidin	Blueberries, Raspberries
Curcuminoid	Curcumin	Turmeric
Stilbene	Resveratrol	Red grapes

<sup>(\*)</sup> Subclasses of Flavonoids