Reviewer's report

Title: Tracing Ancestry With Methylation Patterns: Most Crypts Appear Distantly Related in Normal Adult Human Colon

Authors: Kyoung-Mee Kim (kkmkys@yahoo.co.kr)  
Darryl Shibata (dshibata@hsc.usc.edu)

Version: 1 Date: 25 Aug 2003

Reviewer: Tamostu Sugai

Level of interest: A paper of considerable general medical or scientific interest

Advice on publication: Accept after discretionary revisions

The authors investigated the relationships between methylation patterns in CpG rich loci (methylation %) in various types of human colon crypts. In addition, the differences in methylation sites at two CpG-rich sequences (BGN and CSX sites) were examined in intracrypts and intercrypts. Two types of branched crypts were also analyzed: the crypt with a long trunk and a short branch and the crypt with a short trunk and a long branch. The concept of a Y-shaped tree is useful in tracing the ancestor within the intracrypts.

This carefully performed and detailed study provides good evidence for the results, particularly with regard to clarifying the difference between an intracryptal single crypt and intracryptal branched crypts. In addition, the author confirmed that there was no difference in methylation patterns between intercrypts in the same patch, intercrypts > 15cm apart and adjacent intercrypts. These data are very interesting, as they shed light on the development of human colon crypts. Specific suggestions are given below.

1. The data, though very interesting, are presented in a slightly confusing manner. The definitions of a branched crypt and a Y-shaped tree are very confusing. I believe that Y-shaped trees are not actually observed in colonic mucosa, and they are therefore a theoretical concept, rather than a true category of crypt. Were the authors actually referring to a branched crypt resembling an inverse Y-shaped crypt, which is frequently found in routine inflammatory colonic samples? The authors should clarify the difference between these types of crypt. In addition, the authors should list the picture of a branched crypt as a Figure.

2. In this study, the authors indicated that tag intracrypt distances in branched crypts were significantly greater than in single crypts, and were slightly less than intercrypt distances, but the latter differences did not reach a significant level. Their data suggest that branched crypts represent an intermediate type between intracryptal single crypts and intercrypts. If this is the case, their findings mean that a mature human colon crypt may develop via branched crypts, which are detected in inflammatory colonic mucosa. The authors should state their views regarding development of human colonic crypts in light of their new data.

3. The authors should clarify what A and B indicate in methylation % BGN and intracrypt Distance of Table 1.

Competing interests:

None declared.