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Is There Enough Evidence for the Association of GNβ3 C825T Polymorphism With Functional Dyspepsia and Irritable Bowel Syndrome?

TO THE EDITOR: I read with great interest the paper from the Kim et al[1] on the G-protein beta3 subunit (GNβ3) C825T polymorphism with overlap syndrome of functional dyspepsia (FD) and irritable bowel syndrome (IBS) which demonstrated that no apparent association of the GNβ3 C825T polymorphism with FD, IBS or the overlap of FD and IBS existed. However, a recent study on Korean children showed the CC genotype of GNβ3 C825T may be associated with FD and diarrhea predominant IBS and the TT genotype might be associated with constipation predominant IBS.[2] Since the first study[3] from Germany which indicated homozygous GNβ3 825CC genotype was associated with unexplained predominantly upper abdominal symptoms, many studies[4-13] around the world showed inconsistent results on the association between the GNβ3 C825T polymorphism and functional gastrointestinal disorders (FGIDs). Many factors including heterogeneity of the disease, sample size, sample selection or racial difference may have contributed to these conflicting results. Still, we need to perform further large-scaled well-controlled studies to clarify this unresolved issue.

The GNβ3 C825T polymorphism may change gastrointestinal motor and sensory functions through intracellular signal transduction and biological activity. Camilleri et al[14] showed that GNβ3 T allele was associated with lower fasting gastric volume, which was one of the factors that predicted a portion of the variance in the symptoms of patients with dyspepsia.[15] Further physiologic studies that deal with the effect of the GNβ3 C825T polymorphism on gastrointestinal motor and sensory functions are necessary to clarify the pathophysiologic mechanism in which genetic variations contribute to gastrointestinal symptoms.

Can the GNβ3 C825T polymorphism influence response to therapy in FGIDs? Camilleri et al[16] recently showed that GNβ3 TC/TT genotype might be associated with lower sensations of gas and urgency in response to rectal distention after clonidine treatment in humans. These findings could lead us to select FGIDs patients potentially treatable with clonidine and other drugs, based on genetic variation. Further pharamcogenetic studies could open a new horizon on treating patients with FGIDs in the future.

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Conflicts of interest: None.