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Boston, December 14, 2007

Dear Patient:

With this letter we would like to spark your interest in our research study with the hope to enroll you as a participant. The purpose of our research is to identify the causes of familial forms of hypoparathyroidism.

Familial forms of hypoparathyroidism (where at least 2 members of a family are affected) are a heterogeneous group of disorders that all result in hypoparathyroidism, but the underlying molecular defect can be different from one family to another.

Some of the underlying defects (called "genetic mutations") leading to hypoparathyroidism have already been identified: these are defects in the genes for the calcium-sensing receptor, for parathyroid hormone (PTH) or for the transcription factor GATA3. We have recently identified novel mutations in another protein called GCMB that plays a central role in the formation of parathyroid glands during embryonic development. If this transcription factor is not working properly because of a mutation, parathyroid glands fail to form and hypoparathyroidism ensues.

However, most familial forms of hypoparathyroidism remain unexplained at the molecular level. Our goal is to identify causes of hypoparathyroidism in families without a known mutation in one of the genes mentioned above. The identification of novel gene defects that lead to hypoparathyroidism would provide further inside into this disorder and would help better understand the biology of parathyroid glands.

If you would like to participate, there are two possible involvements:

1. We would first look for mutations in the transcription factor GCMB and other genes known to be involved in hypoparathyroidism (for instance the calcium-sensing receptor and PTH) in your DNA. For that purpose, we would need a single blood sample from you (about 4 teaspoons = 20 cc) that would be shipped to us. We would extract DNA in the laboratory and search for mutations. There are no costs for you involved.

2. If no mutation in known genes can be found, and if you are interested in pursuing additional studies, we would perform a so-called genome-wide screen to look for mutations in novel genes. For that part of the project, we would need a single blood sample from other affected and unaffected members of your family (as many as possible).

Our Institutional Review Board ("IRB") has approved this study; in case you want to participate, please contact us; a consent form will be sent to you and we will call you (or e-mail) to answer any questions you may have.

Please feel free to contact us with any questions that you might be having.

Yours sincerely,

Michael Mannstadt, MD

Harald Jüppner, MD