## CALIFORNIA INSTITUTE OF TECHNOLOGY PASADENA, CALIFORNIA

DIVISION OF BIOLOGY

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Dear Josh,

Fetal Hb is known to differ markedly from normal adult Hb (Hb A) in amino acid composition. For one thing, it contains about 5 times as much isoleucine as Hb A (see Huisman et al., Nature 175, 902, for example). This contrasts with Hb S and the other mutant hemoglobines, whose chemical compositions can be distinguished from normal only by the special methods developed by Ingram.

According to Itano (pers. comm.), the fetal Hb of sickle-cell anemic individuals is normal in its electro-phoretic and other properties. This means that fetal Hb is determined by a different gene from the one that determines Hb A. It seems to be a special protein that is formed in response to anoxia. This would account for its presence in the fetal circulation and in adults with extern either hereditary or acquired anemia.

I don't think you understood my multiple allele argument—certainly I do not understand your reply to it—but I won't labor the point.

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Norman Horowitz