中文題目：Beta 球蛋白基因 IVS-II-81 C>T 不會造成 beta 海洋性貧血

英文題目：**IVS-II-81 C>T in beta-globin gene cannot cause beta-thalassemia**

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Background: Candidates drafted for military service with mean corpuscular volume (MCV) <80 fL and serum ferritin >20 ng/mL were screened for thalassemia. The beta-globin gene (*HBB* gene, location: 11p15.4) provides instructions for making beta-globin which is a compoent of hemoglobin. Although the HbVar database (http://globin.bx.psu.edu/hbvar) provides a lot of information about mutations that cause thalassaemia, many mutations lack well-defined clinical phenotype till now.

Methods: Genomic DNA was extracted from peripheral blood leukocytes using Puregene kit (Gentra Systems, Minneapolis, MN, USA). Gap-PCR and direct sequencing analysis were used for detecting the most common α-thalassemia mutations in Taiwan, including five large sequence deletions ($--^{SEA}$, $--^{FIL}$, $--^{THAI}$, $-\alpha^{3.7}$and $-\alpha^{4.2}$) and two point mutations (the Constant Spring variant and Quong Sze variants). For β-thalassemia, whole *HBB* gene were screened by direct sequencing analysis.

Results: A 22-year-old man with anemia since childhood was referred for constription physical examination. Laboratory tests revealed: red blood cell (RBC) count: 5.19 $\times 10^6$/microL, hemoglobin (Hb): 12.5 g/dL, hematocrit (Hct): 38.0%, MCV: 73.1 fL, white blood cell (WBC) count: 6,200/microL, platelet count: 290×10^3/microL, red blood cell distribution width (RDW): 35.2% (reference range: 11.5 - 14.5%), reticulocyte count: 1.61%; LDH: 160 U/L, direct bilirulin: 0.52 mg/dL, total bilirubin: 1.24 mg/dL, creatinine: 0.92 mg/dL, CRP: 0.03 mg/dL, ferritin: 618.6 ng/mL; Hb electrophoresis: Hb A: 97.1%, Hb A2: 2.9%, Hb H staining: negative; peripheral smear feature: anisocromia, mild hypochromic, and elliptocytes. Molecular analysis showed no mutations for alpha-globin gene, but IVS-II-81 C>T was found in *HBB* gene. His father complete blood count (CBC) results were: Hb: 14.9 g/dL, Hct: 42.7%, MCV: 88.2 fL, WBC count: 6,100/microL, platelet count: 311×10^3/microL; normocytic normochromic RBC. His mother CBC results were: Hb: 13.5 g/dL, Hct: 41.9%, MCV: 87.3 fL, WBC count: 5,600/microL, platelet count: 327×10^3/microL; normocytic normochromic RBC. Molecular analyses of the *HBB* gene were performed in his both parents, and IVS-II-81 C>T was also found in his mother's blood, but no mutation in his father's blood.

Conclusions: We identified IVS-II-81 C>T variant in *HBB* gene in a man with congenital microcytic anemia. His mother was a carrier for this variant, but she had normal CBC results and normal Hb A2 level. According to the information provided on the website of HbVar database, IVS-II-81 C>T is a rare

HBB gene variant in most people of the world except Indian population, and there was no phenotypic and hematologic data available. Our data suggest that the IVS-II-81 C>T in *HBB* gene is not the cause of microcytic anemia, and it cannot cause beta-thalassemia phenotype.