4. VuMathie W 20 cp 5, V.I..da. W N., 2. Carso. P E. Fla. ag~. SelwyaJ G ~ and were found to be deficient in erythro-
hemolytic anemia were recalled for study for the detect. Two brothers with chronic 
daughter and parents had about half of nor-
the erythrocytes of the patient's son and 
this patient; the leukocytes were found to 
have normal activity. We quickly found that 
activity was obtained on the hemolysate of 
chronic anemia. Essentially no P1< enzyme 
Vtadsworth Hospital for investigation of his 
ian veteran who had been admitted to 
P1< assay had been established, I obtained a 
become more readily available.

described as a cause of hemolytic anemia,2 
transmitted as an autosomal 
recessive trait. [The SC indicates that this 
paper has been cited over 265 times since 
1962.] 

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"I am indebted to William Valentine of 
UCLA for providing me, as a junior research 
hematologist, the opportunity in July 1957 
of joining his laboratory located in a 
Quonset hut. In the early fall of 1960, we 
began to set up assays for each enzymatic 
step of the glycolytic pathway to study the 
nonspherocytic hemolytic anemias because 
(1) of Dacie's earlier report on autohemoly-
sis,1 (2) G6PD deficiency had been recently 
described as a cause of hemolytic anemia,3 
and (3) purified enzymes and substrates had 
become more readily available.

"In February 1961, very shortly after the 
PK assay had been established, I obtained a 
sample of blood from a 26-year-old Cauca-
sian veteran who had been admitted to 
Wadsworth Hospital for investigation of his 
chronic anemia. Essentially no PK enzyme 
activity was obtained on the hemolysate of 
this patient; the leukocytes were found to 
have normal activity. We quickly found that 
the erythrocytes of the patient's son and 
daughter and parents had about half of nor-
mal activity consistent with heterozygosity 
for the defect. Two brothers with chronic 
hemolytic anemia were recalled for study 
and were found to be deficient in erythro-

e. The data on these three patients 
were submitted to Science, but the manu-
script was rejected on the basis of lacking 
broad interest.

"Valentine wrote to the president of the 
Association of American Physicians, Cecil J. 
Watson, about our studies on the three sub-
jects. The paper1 was accepted for the an-
nual session in Atlantic City on May 2, 1961, 
less than three months after our initial 
results. A total of seven patients were soon 
found to have a specific deficiency in the 
red cell glycolytic enzyme PK. This formed 
the basis of the manuscript published in 
Blood. Many other cases of PK deficiency 
were soon reported from all over the world.

"Meanwhile, I became chief of hematology 
at Harbor-UCLA Medical Center, and 
have continued to work in the field of red 
cell enzymology and metabolism during the 
past 20 years. However, I collaborated with 
Valentine for a number of years and we still 
write reviews together.4 Miwa, who was a 
research fellow at the time, returned to 
Japan shortly thereafter and has become the 
leading investigator of red cell enzyme defi-
cency hemolytic anemias in Japan.

"The probable reasons for the frequent 
citation of our paper are these. Our initial 
brief paper on PK deficiency was published 
in Transactions of the Association of 
American Physicians,3 but this is not as 
widely circulated as Blood. The paper in 
Blood defined the entity of PK deficiency 
hemolytic anemia, which has proven to be 
the first described, best studied, and most 
common of the hemolytic anemias resulting 
from an enzyme defect in the Embden-Mey-
roth pathway. The discovery of PK defi-
cency excited interest in hereditary 
hemolytic anemias and led to the rapid 
subsequent finding of other enzyme defi-
cency hemolytic anemias, many in Valen-
tine's laboratory.

"The first patient with PK deficiency 
hemolytic anemia has been living for a 
number of years in Sanger, California, where 
I spent the first 15 years of my life. His red 
cell PK enzyme was characterized recently 
and named PK 'Sanger.' "5

1. Selvyn F G & Dickie J V. Autohemolysis and other changes resulting from the incubation in vitro of red cells from 


3. Valentus W N, Tanaka K R & Miwa S. A specific erythrocyte enzyme defect (pyruvate kinase) in three subjects with 


5. Shibahara K & Tanaka K R. Pyruvate kinase deficiency hemolytic anemia. Enzymatic characterization studies in 