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Tarui S, Okuno G, Ikura Y, Tanaka T, Suda M & Nishikawa M.
Phosphofructokinase deficiency in skeletal muscle. A new type of glycogenosis.
Biochem. Biophys. Res. Commun. **19**:517-23, 1965.
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This paper describes a novel entity of glycogenosis due to muscle-type phosphofructokinase deficiency. It also indicates that erythrocyte phosphofructokinase is partially affected, resulting in increased hemolysis in this disease, and suggests the possible existence of isozymes of phosphofructokinase. [The *SCI*® indicates that this paper has been cited in over 190 publications since 1965.]

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"In 1964, I was doing clinical research at the Second Department of Internal Medicine, Osaka University Medical School. My emphasis was on analysis of disorders of carbohydrate metabolism. We were visited by five siblings from a single family, three of whom complained unanimously of quickly induced fatigue and inability to keep pace with their classmates. Since ischemic forearm exercise failed to cause any rise in venous lactate in the three subjects, and their parents were first cousins, we at first thought they were suffering from muscle glycogenosis due to phosphorylase deficiency.

"As I had expected, a significant increase in the glycogen concentration in their muscles was clearly demonstrated. However, completely normal activity of muscle phosphorylase greatly surprised me. Therefore, we had to analyze all the steps below glucose-1-phosphate in the Embden-Meyerhof glycolytic pathway.

"The approximately 60-year history of studies of glycogenosis had taught us that the cooperation of investigators in clinical and basic science fields occasionally bears rich fruit: Wagner-Parnas, von Gierke-Schönheimer, and van Creveld-Huijing are just a few examples. Fortunately, at that time I received much good advice from Tanaka, my classmate in Osaka University Medical School, who was famous for his studies on pyruvate kinase.[1] Consequently, the identification of the defective enzyme was not so difficult. Marked increases in hexose monophosphates and an extreme decrease in fructose-1,6-bisphosphate in muscles indicated the distinct crossover in the phosphofructokinase step.

"Of interest was the fact that erythrocyte phosphofructokinase was only partially affected in contrast to the almost complete lack of muscle phosphofructokinase activity. It provided a challenge for further intensive study of the isozymes of phosphofructokinase.[2,3] These fundamental features of the disease have been confirmed by many case studies reported in the US, France, England, Canada, Spain, and Italy.[4]

"This clinical entity was classified as Type VII glycogenosis by Brown and Brown.[5] No controversy has hitherto occurred concerning the eponym. At present, Type VII glycogenosis (Tarui disease) is not infrequently described in textbooks of metabolism, hematology, neurology, biochemistry, internal medicine, and pediatrics.

"The popularity of this paper seems to rest on the following points. First, it added a novel clinical entity not only to glycogenosis but also to enzymopenic hemolytic anemia. Second, the defective enzyme demonstrated is nothing else but phosphofructokinase, which plays a key regulatory role in glycolysis through its complicated allosteric properties. Third, it provided the indication of the possible existence of the isozymes of phosphofructokinase and also gave an impetus to the study of phosphofructokinase in a number of nonhuman mammalian species.[3] Finally, it represented a unique experiment of nature and could open a new way to the understanding of the cause of alterations in glycolytic intermediates, e.g., the close relationship between phosphofructokinase and 2,3-bisphosphoglycerate in erythrocytes."[6]

1. **Tanaka T, Harano Y, Sue F & Morimura H.** Crystallization, characterization and metabolic regulation of two types of pyruvate kinase isolated from rat tissues. *J. Biochem. Tokyo* **62**:71-91, 1967. (Cited 420 times.)
2. **Tarui S, Kono N, Nasu T & Nishikawa M.** Enzymatic basis for the coexistence of myopathy and hemolytic disease in inherited muscle phosphofructokinase deficiency. *Biochem. Biophys. Res. Commun.* **34**:77-83, 1969. (Cited 75 times.)
3. **Vora S.** Isozymes of phosphofructokinase. *Curr. Top. Biol. Med. Res.* **6**:119-67, 1982.
4. **Tarui S, Mineo I, Shimizu T, Sumi S & Norio K.** Muscle phosphofructokinase deficiency and related disorders. (Serratrice G, Cros D, Desnuelle C, Gastaut J L, Pellissier J F, Pouget J & Schiano A, eds.) *Neuromuscular diseases*. New York: Raven Press, 1984. p. 71-6.
5. **Brown I B & Brown D H.** Glycogen-storage diseases: type I, III, IV, V, VII and unclassified glycogenosis. (Deckens F, Randle P J & Whelan W J, eds.) *Carbohydrate metabolism and its disorders*. London: Academic Press, 1968. Vol. 2. p. 123-50.
6. **Tarui S, Kono N, Kuwajima M & Kitani T.** Hereditary and acquired abnormalities in erythrocyte phosphofructokinase activity. The close association with altered 2,3-diphosphoglycerate levels. *Hemoglobin* **4**:581-92, 1980.

