To the Editor:

The paper by Sassa et al. might lead to the conclusion that the only erythropoietic response to Friend virus is polycythemia. This is not the case. Polycythemia was first noted with the Mirand strain of Friend virus, but anemia consistently develops following infection with the Rich and Brodsky strains. Furthermore, the naturally infected offspring of mice infected with Mirand's strain do not develop polycythemia but rather a pronounced and progressive anemia. The polycythemic response can be abolished and the anemia potentiated by splenectomy. Rauscher virus, which is virtually identical to Friend virus, causes only an anemia that is also more severe after splenectomy. The anemia following both Friend and Rauscher virus infection is due to hemolysis and represents a non-neoplastic manifestation of a leukemia virus infection. The spleen can compensate in part for the hemolysis by increasing its production of RBC. The mechanism for the polycythemia following infection with certain strains of Friend virus is not clear. It may represent the presence of two viral agents in the inoculum—one causing a polycythemia and the other agent, a lymphocytic leukemia. Another explanation is that in certain strains of mice the spleen overcompensates, perhaps in response to an erythropoietin-like substance, and polycythemia develops. Sassa et al., also speculated on the possibility of a similarity in action between erythropoietin and Friend virus. It has already been demonstrated that the Mirand strain, like erythropoietin, is capable of reestablishing erythropoiesis in the hyper-transfused-polycythemic state but this cannot be accomplished with those strains of Friend virus and Rauscher virus that cause a hemolytic anemia.

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REFERENCES

To the Editor:

Thank you for permitting me to comment on Dr. Brodsky’s “Letter to the Editor” concerning our recent paper in Blood1 on the polycythemic response of ddO mice to infection with the Friend virus. It was not the intent of the paper to conclude, as Dr. Brodsky appears to have done, that the only erythropoietic response to this virus in the mouse is polycythemia. The important features of our paper are the facts that Friend leukemia virus in the particular species studied produced a marked increase in the erythropoiesis which led to a polycythemia in the affected mice, and that the increased erythropoietic activity was not suppressed by hypertransfusion; also, that the plasma and spleen extract of the Friend virus-infected animal showed no erythropoietin activity. From these facts, we postulated that erythropoiesis in Friend leukemia in ddO mice is not governed by erythropoietin production and that possibly the Friend virus, substituted for erythropoietin, thus causing an uncontrolled differentiation of erythroid precursors sufficient to produce polycythemia.

In some strains in a previous experiment, the increased erythropoiesis in Friend leukemia has been attributed to a hemolytic anemia.2 The possibility of hemolysis in Friend leukemia cannot be denied, however, erythropoiesis sufficient to cause polycythemia is not likely to be merely a result of such hemolytic anemia for the following reasons: 1) ddO mice which are affected by Friend virus have never been shown to pass through an anemic phase preceding the marked polycythemia, and 2) if the increased erythropoiesis in such animal is due to a hemolytic anemia, hypertransfusion would be expected to suppress the increased erythropoiesis; however, this is not the case in our study. Brodsky et al.2 have found a shortening of red cell survival in Swiss Webster mouse infected with Friend Leukemia virus, by labeling of red cell with radiocromate; on the other hand, Mirand et al.3 stated that red cell destruction in Ha/ICR Swiss mouse was within the normal range with 51Cr labeling.

The reason why some strains of Friend virus cause polycythemia and others produce anemia is not understood. We feel that such differences in responses suggest the presence of more than one related virus in the so-called Friend virus,3 or that these differences may be due to different host responses to a murine leukemia virus.4

After submitting our paper, it came to our attention that Mirand reported that Friend virus (Mirand strain), like erythropoietin, could release the inhibition of erythropoiesis during the hypertransfused-polycythemic state3 although more recently, the same author reported that “the polycythemic virus” acted like erythropoietin in the hypertransfused mouse, but that Friend virus did not.5

Our results have shown that hypertransfusion in Friend virus-affected ddO mouse does not suppress erythropoiesis at all; and it could therefore be
suggested that the erythropoiesis in Friend leukemia-infected dd0 mouse is not governed by a normal mechanism.

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REFERENCES