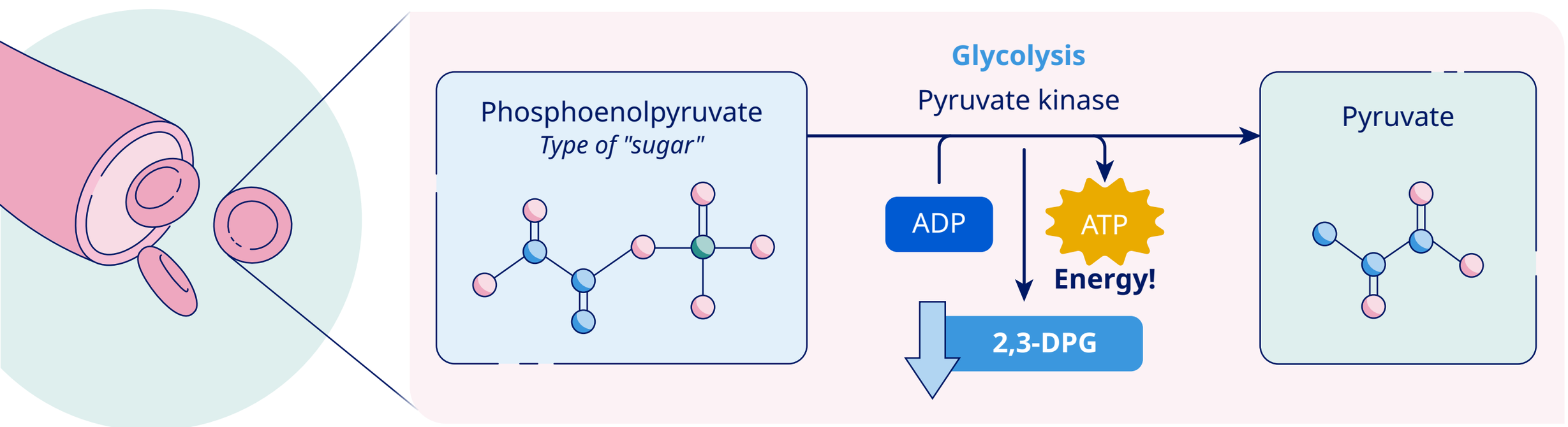
PKR activators are investigational. Safety and efficacy are not established. There is no guarantee that investigational PKR activators will become commercially available for the use(s) under investigation.

Restoring energy balance and improving oxygen delivery throughout the body: The potential dual roles of PKR activators in red blood cells

The importance of PKR activation to red blood cell health[1–4]

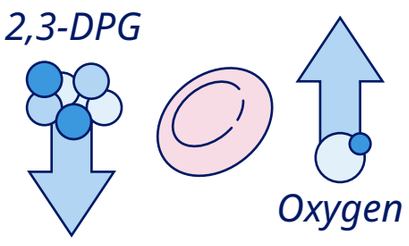
All the cells in your body need to produce energy to carry out their functions, including your red blood cells. Pyruvate kinase (PKR) is an enzyme present in red blood cells that helps turn sugar into energy in a reaction called glycolysis.[1] In this reaction, activation of PKR converts the sugar phosphoenolpyruvate into pyruvate, and in the process creates ATP (adenosine triphosphate), which is the energy used by cells to function and fuel red blood cells to carry oxygen from the lungs to the rest of the body. The glycolysis reaction also lowers the levels of 2,3-DPG (2,3-diphosphoglycerate), a compound that decreases the red blood cell's ability to hold and transport oxygen.[2–4]



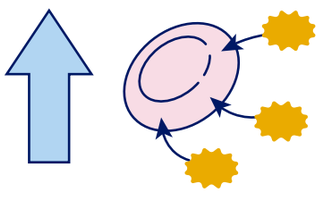
What is the role of PKR in sickle cell disease?[2–5]

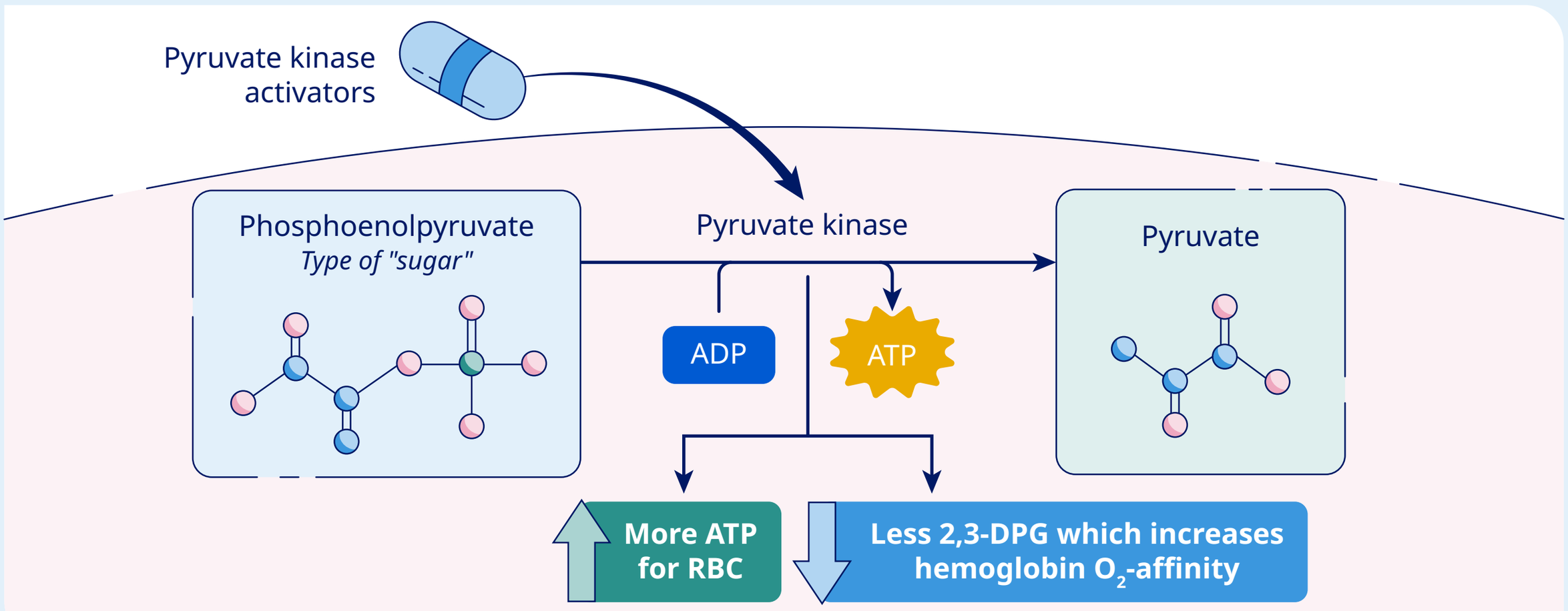
In sickle cell disease, lack of oxygen transport to organs is a major contributor to many of the complications experienced by patients, and treatments for this can potentially improve symptoms of the disease. Using a dual mechanism, PKR activators may be able to treat sickle cell disease by:

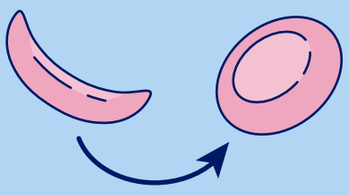
1 Reducing 2,3-DPG build up and increasing oxygen binding



2 Increasing the levels of ATP (energy) inside of the red blood cells[5]





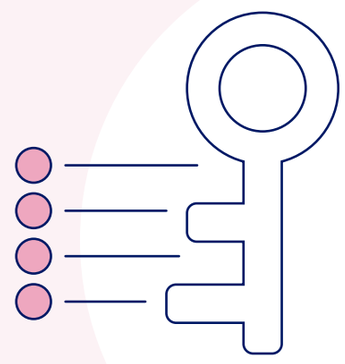


PKR activation decreases hemoglobin sickling and repairs red blood cells

Activation of PKR in sickled cells may be able to restore the energy balance within the red blood cells, reduce hemoglobin sickling by increasing oxygen binding, and therefore improve the delivery of oxygen throughout the body.[2–4] Based on this information, PKR activators are a potential investigational therapy in the treatment of sickle cell disease.

Key Takeaways

- PKR is an enzyme present in red blood cells that helps turn sugar into energy and allows the cells to carry oxygen from the lungs to the rest of the body
- Activating PKR in sickle cell disease enhances glycolysis to reduce 2,3-DPG levels and increase energy production, thereby improving red blood cell health and reducing sickling
- PKR activators are an investigational treatment that may treat sickle cell disease by through a dual mechanism: (1) restoring energy balance in red blood cells, and (2) reducing cell sickling and improving oxygen delivery throughout the body



1. Schroeder P et al. J Pharmacol Exp Ther 2022;380(3):210–219. doi: 10.1124/jpet.121.000743; 2. Grace RF et al. Br J Haematol 2019;184(5):721–734. doi: 10.1111/bjh.15758; 3. Matte A et al. Curr Opin Hematol 2023;30(3);93–98. doi: 10.1097/MOH.0000000000000758; 4. Glenthøj A. haematologica 2024:109(8): doi: 10.3324/haematol.2024.285390; 5. Xu JZ and Vercellotti GM. Hematology Am Soc Hematol Educ Program 2023;2023(1):107–113.