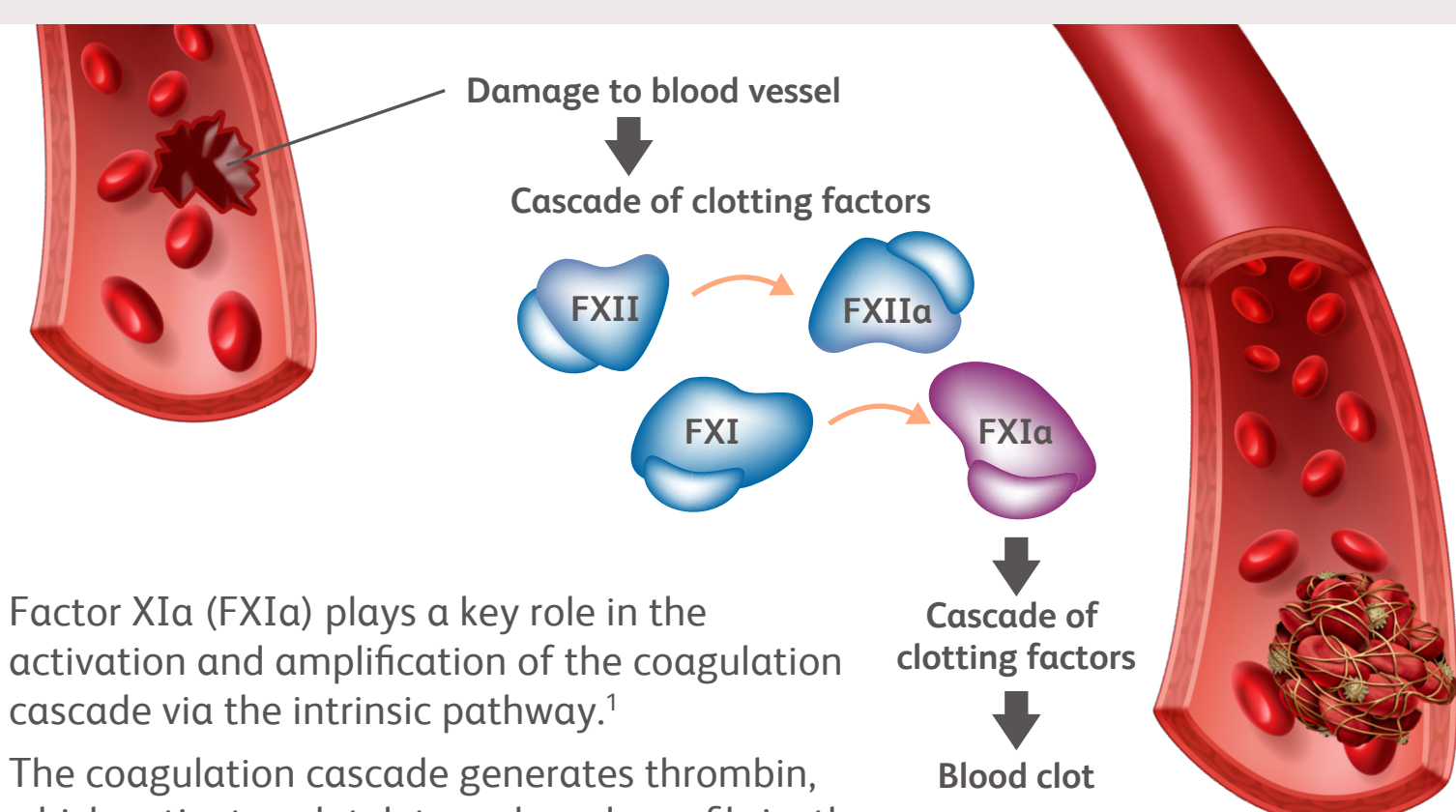


Factor XIa (FXIa)

About Factor XIa



Factor XIa (FXIa) plays a key role in the activation and amplification of the coagulation cascade via the intrinsic pathway.¹

The coagulation cascade generates thrombin, which activates platelets and produces fibrin, the structural backbone of a thrombus or blood clot.

Normal coagulation is essential to maintaining hemostasis, which prevents blood loss in case of illness or injury.

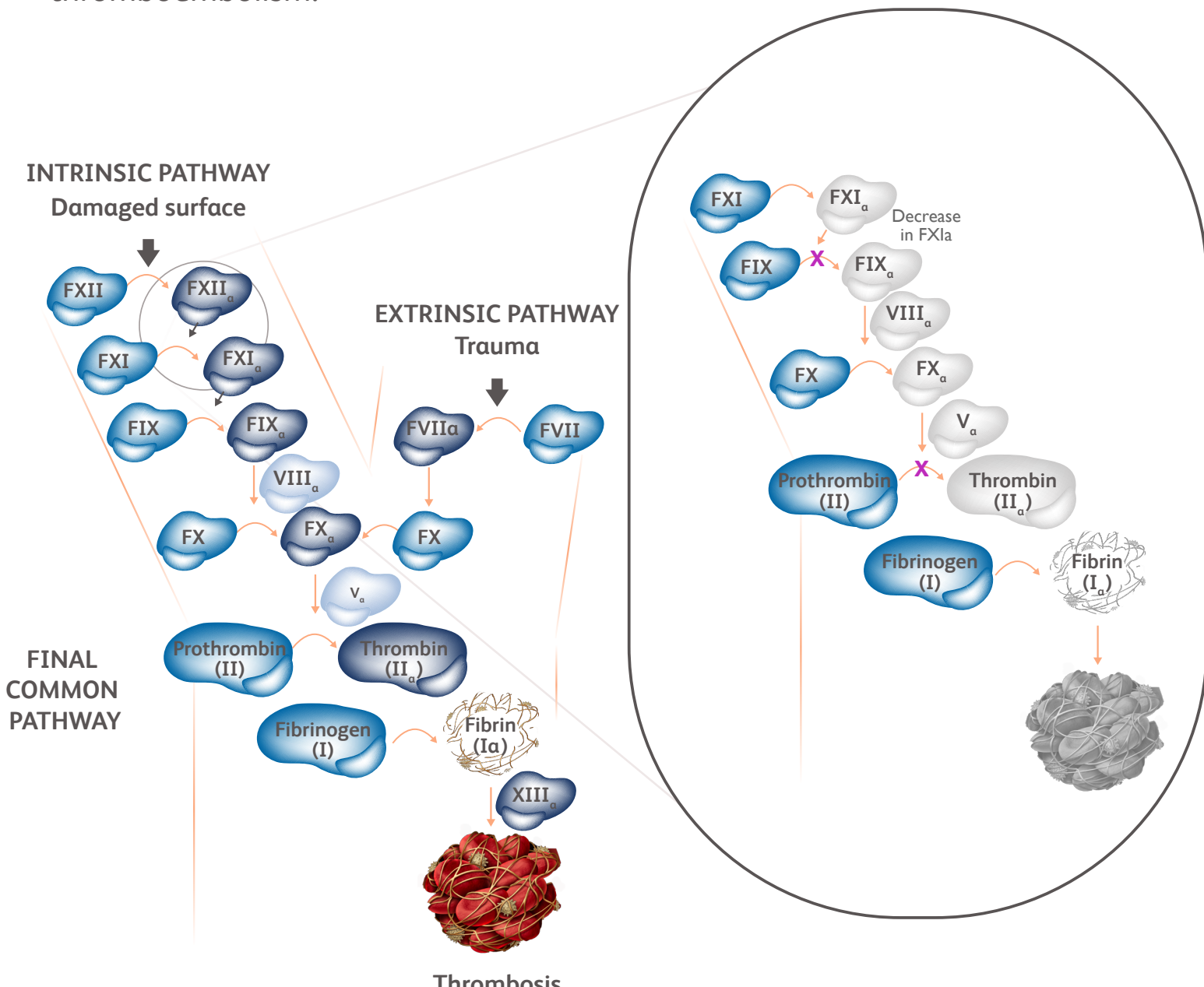
Factor XIa and Thrombosis

- Thrombosis is the pathophysiological state in which the coagulation cascade is inappropriately activated and there is an increased level of thrombin.² Thrombosis is the most immediate cause of many types of heart attack, stroke and peripheral artery disease.
- The coagulation cascade has two separate triggers, the extrinsic and intrinsic pathways, which converge on a common pathway that generates thrombin.
- The active form of FXIa is produced via the intrinsic pathway as factors in the cascade upstream of Factor XI (FXI) are enzymatically cleaved and activated. As an amplification mechanism, FXI is also activated by thrombin in a feedback activation loop. The amplification mechanism is believed to be more important for thrombosis than hemostasis. FXIa is positioned upstream in the cascade and connects the intrinsic pathway activation and feedback amplification loop to the common pathway of coagulation by converting FXI to FXIa.

Research Implications

FXIa was first noticed as a potential approach to thrombosis because people with little or no FXIa (Hemophilia C) show virtually no untoward bleeding in the absence of a major injury or surgery.

Further, a small study of Hemophilia C patients showed a lower risk of stroke. Conversely, elevated levels of FXI/FXIa is a risk factor for stroke and venous thromboembolism.



Rooted in a long-term commitment to patients with cardiovascular disease, Bristol Myers Squibb is committed to advancing research in the area of prevention for stroke and other related conditions. Learn more about our work here: <https://www.bms.com/researchers-and-partners/areas-of-focus.html>

1. R. Al-Horani, et al. Factor XIa inhibitors: A review of patent literature. *Expert Opin Ther Pat.* 2016; 26(3): 323-345.

2. Z. Hu, et al. Discovery of a Potent Parenterally Administered Factor XIa Inhibitor with Hydroxyquinolin-2(1H)-one as the P2' Moiety. *ACS Med Chem Lett.* 2015 May 14; 6(5): 590-595.