

# Mechanisms in Thrombosis and Hemostasis

## Prof. Yona Nadir Lab

### Coagulation – a physiological system interfacing all other body systems

The coagulation system is a rapidly advancing area of clinical and basic research. Extensive research in the challenging field of thrombosis and bleeding is ongoing and has already resulted in new pharmacological modalities such as siRNA technology based drugs. There is a vicious cycle between the coagulation system and infection, inflammation, cancer and angiogenesis. The well-established strong association between coagulation and cancer provides a solid incentive for developing drugs capable to interfere with the coagulation system to attenuate tumor growth.

### We are looking for talented motivated students for MSc, PhD positions

Contact:

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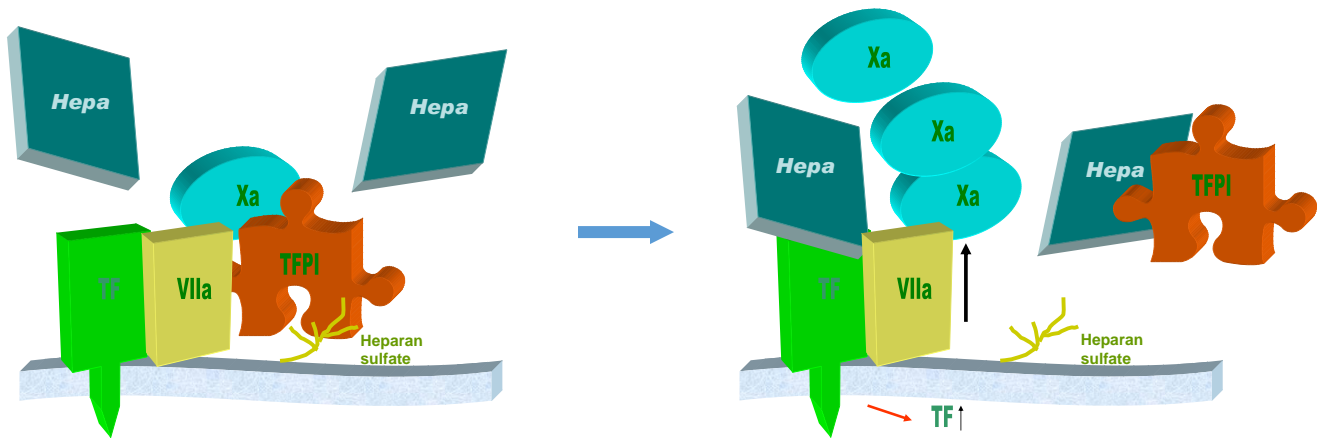
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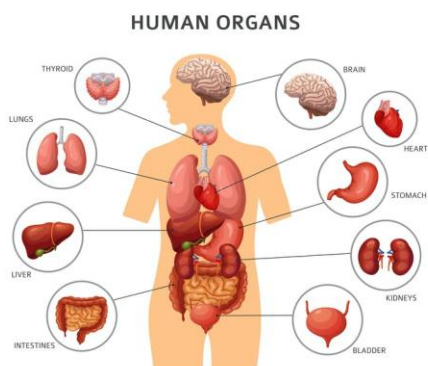
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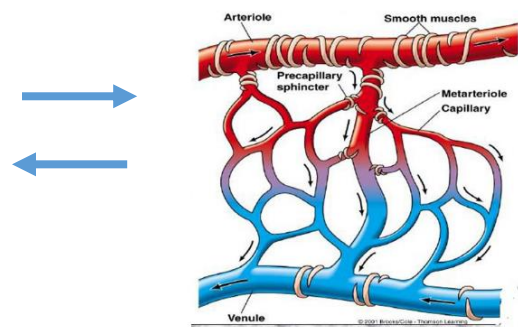




**A model of the interaction between heparanase (Hepa), TF, and TFPI.** Heparanase interacts with tissue factor (TF) resulting in increased generation of factor Xa and enhancement of the coagulation system. Heparanase also up-regulates TF expression and releases tissue factor pathway inhibitor (TFPI) from the cell surface, rendering the cell surface highly pro-coagulant. TFPI and heparanase may circulate as a complex in the plasma.



The microcirculation



**Organs microcirculation hemostatic niche.** Reciprocal effect of the microcirculation hemostasis in the specific organ.

## Main topics in recent years:

- E. Axelman, I. Henig, Y. Crispel, J. Attias, JP. Li, B. Brenner, I. Vlodaysky, **Y. Nadir**. Novel peptides that inhibit heparanase activation of the coagulation system. *Thromb Haemost.* 2014, 112:666-77.
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- E. Peled, E. Melamed, T. Banker Portal, E. Axelman, D. Norman, B. Brenner, **Y. Nadir**. Heparanase procoagulant activity as a predictor of wound necrosis following diabetic foot amputation. *Thromb Res.* 2016, 139:148-53.
- Y. Crispel, E. Axelman, M. Tatour, I. Kogan, N. Nevo, B. Brenner, **Y. Nadir**. Peptides inhibiting heparanase procoagulant activity significantly reduce tumor growth and vascularization in a mouse model. *Thromb Haemost.* 2016, 116:669-78.
- M. Tatour, M. Shapira, E. Axelman, A. Keren-Politansky, L. Bonstein, B. Brenner, **Y. Nadir**. Thrombin is a selective inducer of heparanase release from platelets and granulocytes via protease activated receptor-1. *Thromb Haemost.* 2017, 117: 1391-1401.
- Y. Crispel, S. Ghanem, J. Attias, I. Kogan, B. Brenner, **Y. Nadir**. Involvement of heparanase procoagulant domain in bleeding and angiogenesis. *J Thromb Haemost.* 2017, 15:1463-1472.
- N. Nevo, S. Ghanem, Y. Crispel, M. Tatour, I. Kogan, M. Ben-Harush, **Y. Nadir**. Heparanase level in the microcirculation as a possible modulator of the metastatic process. *Am J Pathol.* 2019, 189:1654-1663.
- E. Hardak, E. Peled, Y. Crispel, S. Ghanem, J. Attias, K. Asayag, I. Kogan, **Y. Nadir**. Heparan sulfate chains contribute to the anticoagulant milieu in malignant pleural effusion. *Thorax.* 2020, 75:143-152.
- C. Maurice-Dror, M. Litvak, A. Keren-Politansky, S. Ackerman, N. Haim, **Y. Nadir**. Circulating heparan sulfate chains and weight contribute to anti-Xa levels in cancer patients using the prophylactic dose of enoxaparin. *J Thromb Thrombolysis.* 2020, 50:112-122.
- S. Treger, S. Ackerman, V. Kaplan, S. Ghanem, **Y. Nadir**. Progesterone type affects the increase of heparanase level and pro-coagulant activity mediated by the estrogen receptor. *Human Reproduction.* 2021, 36:61-69
- H. Ghoti, S. Ackerman, S. Rivella, C. Casu, **Y. Nadir**. Heparanase level and procoagulant activity are increased in thalassemia major and attenuated by JAK-2 inhibition. *Am J Pathol.* 2020, 190:2146- 2154.