

BÖLÜM 28



GLİKOPROTEİN IIb/IIIa İNHİBİTÖRLERİ

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GİRİŞ

Trombosit aktivasyonu, farklı görevlere sahip çok sayıda protein molekülünün trombosit üzerinde bulunan reseptörlerle bağlanmasıyla gerçekleşir. Bunlar içinde Glikoprotein (GP) IIb/IIIa reseptör proteini trombosit yüzeyinde en yoğun olan蛋白质idir. İnaktif trombosit hücre yüzeyinde yaklaşık 50 ila 80 bin GP IIb/IIIa reseptörü bulunduğu tahmin edilmektedir.¹ GP IIb/IIIa reseptörleri, hücreler arasında etkileşim sağlayan integrinler ailesindendir. Integrin reseptörleri hücre-hücre ve/veya hücre-matriks etkileşimini sağlarlar. Alfa ve beta sub-ünitelerinden oluşur.² GP IIb/IIIa reseptörü, trombosit agregasyonunun uyarılmasında önemli bir rol oynar. Hangi yolaktan ilerlerse ilerlesin trombosit aktivasyonu ve agregasyonunun, son olayı fibrinojen molekülünün GP IIb/IIIa reseptörüne bağlanmasıdır. Bu aşamada trombositlerde oluşan agregasyon GP IIb/IIIa reseptörlerinde bulunan proteinlerde değişime sebep olarak fibrinojene bağlanmaya olanak sağlar. Reseptörün bu fonksiyonunun engellenmesi, akut koroner sendrom (AKS) tedavisi için mükemmel hedef oluşturmaktadır.^{3,4}

GP IIb/IIIa reseptör antagonistinin varoluşu murin monoklonal antikorların keşfi başlamış ve sonrasında, trombosit agregasyonunun düşük doz bağımlı ADP inhibityonuna dikkat yönlendirilmiştir. Bir şimerik monoklonal antikor fragmanı absikimab GP IIb/IIIa reseptör kompleksini fibrinojen ve von Willebrand faktörünün bağlanması engelleyerek inhibe eder. Eptifibatid ve tirofibin GP IIb/IIIa reseptörünün bloke edilmesi de absikimaba benzer şekilde gerçekleşir. Eptifibatid,

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KAYNAKLAR

1. Whalen KFRPTA. Lippincott's illustrated reviews : pharmacology. Philadelphia, Pa.: Wolters Kluwer; 2015.
2. Hynes RO. Integrins: a family of cell surface receptors. *Cell*. 1987;48(4):549-54.
3. Pytela R, Pierschbacher MD, Ginsberg MH, Plow EF, Ruoslahti E. Platelet membrane glycoprotein IIb/IIIa: member of a family of Arg-Gly-Asp-specific adhesion receptors. *Science*. 1986;231(4745):1559-62.
4. Phillips DR, Charo IF, Parise LV, Fitzgerald LA. The platelet membrane glycoprotein IIb-IIIa complex. *Blood*. 1988;71(4):831-43.
5. Hurst JWFVWRAHRA. Hurst's the heart. Vol. 1 Vol. 1. New York: McGraw-Hill Medical; 2011.
6. Roffi M, Patrono C, Collet JP, et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). *Eur Heart J*. 2016;37(3):267-315.
7. Reverter JC, Beguin S, Kessels H, Kumar R, Hemker HC, Coller BS. Inhibition of platelet-mediated, tissue factor-induced thrombin generation by the mouse/human chimeric 7E3 antibody. Potential implications for the effect of c7E3 Fab treatment on acute thrombosis and "clinical restenosis". *J Clin Invest*. 1996;98(3):863-74.
8. Coller BS, Folts JD, Scudder LE, Smith SR. Antithrombotic effect of a monoclonal antibody to the platelet glycoprotein IIb/IIIa receptor in an experimental animal model. *Blood*. 1986;68(3):783-6.
9. Punjabi PP. Book Review: Opie's Cardiovascular Drugs: A Companion to Braunwald's Heart Disease. *Perfusion*. 2021;36(7):772-.
10. Topol EJ, Califf RM, Weisman HF, et al. Randomised trial of coronary intervention with antibody against platelet IIb/IIIa integrin for reduction of clinical restenosis: results at six months. The EPIC Investigators. *Lancet*. 1994;343(8902):881-6.
11. Investigators E. Platelet glycoprotein IIb/IIIa receptor blockade and low-dose heparin during percutaneous coronary revascularization. *N Engl J Med*. 1997;336(24):1689-96.
12. Randomised placebo-controlled trial of abciximab before and during coronary intervention in refractory unstable angina: the CAPTURE Study. *Lancet*. 1997;349(9063):1429-35.
13. Prioli KM, Karp JK, Lyons NM, Chrebtow V, Herman JH, Pizzi LT. Economic Implications of Pathogen Reduced and Bacterially Tested Platelet Components: A US Hospital Budget Impact Model. *Appl Health Econ Health Policy*. 2018;16(6):889-99.
14. Kastrati A, Mehilli J, Neumann FJ, et al. Abciximab in patients with acute coronary syndromes undergoing percutaneous coronary intervention after clopidogrel pretreatment: the ISAR-REACT 2 randomized trial. *JAMA*. 2006;295(13):1531-8.
15. De Carlo M, Maselli D, Cortese B, et al. Emergency coronary artery bypass grafting in patients with acute myocardial infarction treated with glycoprotein IIb/IIIa receptor inhibitors. *Int J Cardiol*. 2008;123(3):229-33.
16. Tcheng JE. Impact of eptifibatide on early ischemic events in acute ischemic coronary syndromes: a review of the IMPACT II trial. *Integrilin to Minimize Platelet Aggregation and Coronary Thrombosis*. *Am J Cardiol*. 1997;80(4A):21B-8B.
17. Platelet Glycoprotein IIb/IIIa UARSUITTI. Inhibition of platelet glycoprotein IIb/IIIa with eptifibatide in patients with acute coronary syndromes. *N Engl J Med*. 1998;339(7):436-43.
18. Gibson CM, Goel M, Cohen DJ, et al. Six-month angiographic and clinical follow-up of patients prospectively randomized to receive either tirofiban or placebo during angioplasty in the RESTORE trial. *Randomized Efficacy Study of Tirofiban for Outcomes and Restenosis*. *J Am Coll Cardiol*. 1998;32(1):28-34.
19. Platelet Receptor Inhibition in Ischemic Syndrome Management Study I. A comparison of aspirin plus tirofiban with aspirin plus heparin for unstable angina. *N Engl J Med*. 1998;338(21):1498-505.
20. Platelet Receptor Inhibition in Ischemic Syndrome Management in Patients Limited by Unstab-

- le S, Symptoms Study I. Inhibition of the platelet glycoprotein IIb/IIIa receptor with tirofiban in unstable angina and non-Q-wave myocardial infarction. *N Engl J Med.* 1998;338(21):1488-97.
- 21. Zhao XQ, Theroux P, Snapinn SM, Sax FL. Intracoronary thrombus and platelet glycoprotein IIb/IIIa receptor blockade with tirofiban in unstable angina or non-Q-wave myocardial infarction. Angiographic results from the PRISM-PLUS trial (Platelet receptor inhibition for ischemic syndrome management in patients limited by unstable signs and symptoms). PRISM-PLUS Investigators. *Circulation.* 1999;100(15):1609-15.
 - 22. Gold HK, Garabedian HD, Dinsmore RE, et al. Restoration of coronary flow in myocardial infarction by intravenous chimeric 7E3 antibody without exogenous plasminogen activators. Observations in animals and humans. *Circulation.* 1997;95(7):1755-9.
 - 23. Combining thrombolysis with the platelet glycoprotein IIb/IIIa inhibitor lamifiban: results of the Platelet Aggregation Receptor Antagonist Dose Investigation and Reperfusion Gain in Myocardial Infarction (PARADIGM) trial. *J Am Coll Cardiol.* 1998;32(7):2003-10.
 - 24. Giugliano RP, Antrnan EM, McCabe CH, et al. Abciximab + tPA improves coronary flow in a wide range of subgroups: Results from TIMI Circulation 1998;98:1- 560.
 - 25. Collet J-P, Thiele H, Barbato E, et al. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: The Task Force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). *European Heart Journal.* 2020;42(14):1289-367.
 - 26. Neumann F-J, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. *European Heart Journal.* 2018;40(2):87-165.