CHEMICAL REVIEWS

Addition/Correction

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Correction to Leukotriene Receptors

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The authors provide this addition to correct the omission of key references in the original review.

1. PAGE 6245, SECTION 3.5.1, LEFT COLUMN, LINE 5 FROM TOP

Thereafter, Basu et al. determined the critical residues in human BLT1 for the LTB_4 binding and receptor activation.[1] They demonstrated that Ala substitutions for His94 and Tyr102 in TM3, Glu185 in TM5, and Asn241 in TM6 in human BLT1 led to the impairment of the LTB_4 binding. Moreover, they found that Arg156 in extracellular loop 2 (EL2) is also required for the LTB_4 binding. In silico molecular dynamics simulations for the ligand-free and ligand-bound states of human BLT1 revealed that the core domain for the receptor activation is formed around Asp64 in TM2, interacting with Asn36 in TM1, Ser100 in TM3, and Asn281 and a triad of Ser residues, Ser277, Ser278, and Ser279, in TM7. Although many of the receptors with a mutation in these residues showed similar LTB_4 binding to wild-type BLT1, these mutants did not evoke the signaling. Thus, these data suggest that the polar residues in TM3, TM5, and TM6 and EL2 are required for the LTB_4 binding; in contrast, the polar residues in TM1, TM2, TM3, and TM7 are crucial for the BLT1 activation.

(1) Basu, S.; Jala, V. R.; Mathis, S.; Rajagopal, S. T.; Del Prete, A.; Maturu, P.; Trent, J. O.; Haribabu, B. *J. Biol. Chem.* **2007**, *282*, 10005.

2. PAGE 6252

Section 3.9, left column, line 5 from top

In vivo, the treatment with BLT1 antagonists effectively reduced the development of inflammation. Moreover, the significant amount of LTB_4 was detected in inflammatory exudates, indicating the pivotal roles of the LTB_4−BLT1 axis in this disease.[1]

(1) Jala, V. R.; Haribabu, B. *Trends Immunol.* **2004**, *25*, 315.

Section 3.9, left column, line 13 from top

On the basis of these findings, many pharmaceutical companies have developed various inhibitors for LTB_4 synthetic enzymes and antagonists for cognate receptors.

Section 3.9.1, left column, line 18 from top

So far, the analyses of 5-LO-null and LTA_4 hydrolase-null mice revealed the crucial roles of LTB_4 in inflammation.[1−6]

(1) Chen, X. S.; Sheller, J. R.; Johnson, E. N.; Funk, C. D. *Nature* **1994**, *372*, 179.

(2) Goulet, J. L.; Snouwaert, J. N.; Latour, A. M.; Coffman, T. M.; Koller, B. H. *Proc. Natl. Acad. Sci. U.S.A.* **1994**, *91*, 12852.

(3) Griffiths, R. J.; Smith, M. A.; Roach, M. L.; Stock, J. L.; Stam, E. J.; Milici, A. J.; Scampoli, D. N.; Eskra, J. D.; Byrum, R. S.; Koller, B. H.; McNeish, J. D. *J. Exp. Med.* **1997**, *185*, 1123.

(4) Irvin, C. G.; Tu, Y. P.; Sheller, J. R.; Funk, C. D. *Am. J. Physiol.* **1997**, *272*, L1053.

(5) Byrum, R. S.; Goulet, J. L.; Snouwaert, J. N.; Griffiths, R. J.; Koller, B. H. *J. Immunol.* **1999**, *163*, 6810.

(6) Jala, V. R.; Haribabu, B. *Trends Immunol.* **2004**, *25*, 315.

Section 3.9.1, right column, line 4 from top

Recently, Haribabu et al. found that the female BLT1-null mice are protected from the PAF-induced anaphylaxis compared with male mice.[1,2] A similar sex-related difference was observed in the mouse strain MRL-lpr/lpr, which shows the accelerated mortality of male 5-LO-null mice compared with male wild-type animals.[3] The reasons for these differences are still unclear. Analyses of BLT1-null mice revealed the significance of the LTB_4−BLT1 axis in the recruitment of various inflammatory cells such as T-cells.[4−6]

(1) Haribabu, B.; Verghese, M. W.; Steeber, D. A.; Sellars, D. D.; Bock, C. B.; Snyderman, R. *J. Exp. Med.* **2000**, *192*, 433.

(2) Jala, V. R.; Haribabu, B. *Trends Immunol.* **2004**, *25*, 315.

(3) Goulet, J. L.; Griffiths, R. C.; Ruiz, P.; Spurney, R. F.; Pisetsky, D. S.; Koller, B. H.; Coffman, T. M. *J. Immunol.* **1999**, *163*, 359.

(4) Goodarzi, K.; Goodarzi, M.; Tager, A. M.; Luster, A. D.; von Andrian, U. H. *Nat. Immunol.* **2003**, *4*, 965.

(5) Ott, V. L.; Cambier, J. C.; Kappler, J.; Marrack, P.; Swanson, B. J. *Nat. Immunol.* **2003**, *4*, 974.

(6) Tager, A. M.; Bromley, S. K.; Medoff, B. D.; Islam, S. A.; Bercury, S. D.; Friedrich, E. B.; Carafone, A. D.; Gerszten, R. E.; Luster, A. D. *Nat. Immunol.* **2003**, *4*, 982.

3. PAGE 6253, SECTION 3.9.3, LEFT COLUMN

3.9.3. Atherosclerosis

So far, several lines of evidence have revealed the involvement of the LTB_4−BLT1 axis in the development of atherosclerosis.[1] In 2002, Mehrabian et al. identified a gene locus on mouse chromosome 6 involved in the resistance to atherogenesis with the mouse strain CAST and determined 5-LO in this locus as a responsible gene for this phenotype.[2,3] They further demonstrated that 5-$LO^{+/-}$ in the low-density lipoprotein receptor (LDLR)-null background showed moderate atherogenesis, suggesting the crucial contribution of 5-LO to this process.[2,3] Moreover, a genome-wide scan analyses in Iceland and U.K. found that FLAP (ALOX5AP) gene is linked to the risk for myocardial infarction (MI) and stroke.[4] Jawien et al. recently reported that the treatments with FLAP inhibitors, MK-886 and DG-031 (also known as Bay-X-1005), attenuate the development of atherosclerosis in apo-E/LDLR-double null mice.[5,6] Interestingly, DG-031 reduced the levels of biomarkers, serum C-reactive protein and amyloid-A, in MI patients with specific at-risk variants in either FLAP or LTA_4 hydrolase gene.[7] These

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data further support the implication of 5-LO in the development of this disease.[8,9] Various LT receptors are expressed in HUVECs, macrophages, smooth muscle, and activated T-cells.[10−12] Moreover, the human vascular lesions could produce LTs, including LTB_4, supporting their involvement in atherogenesis.[1,13] Aiello et al. showed that BLT1-antagonist (CP-105,696) significantly decreases the lesions in both apo-E-null and LDLR-null mice.[14] Interestingly, Subbarao et al. reported that BLT1-null mice in apo-E-null background showed significant reduction in the lesions when these mice were fed a high-fat diet for 4 and 8 weeks, although these reductions were not observed when mice were fed the same diet for 19 weeks.[15] It is still unclear why they could not observe the resistance in the latter condition. Recently, Gennaro et al. reported the enhanced expression of LTC_4 synthase in human abdominal aortic aneurysms (AAAs).[16] They further confirmed the biosynthesis of LTC_4 and inhibition of the LTC_4-induced matrix metalloprotease release by CysLT1 antagonist (montelukast) in human AAAs, suggesting the implication of other LTs and cognate receptors in this disease.

(1) Jala, V. R.; Haribabu, B. *Trends Immunol.* **2004**, *25*, 315.

(2) Mehrabian, M.; Allayee, H.; Wong, J.; Shih, W.; Wang, X. P.; Shaposhnik, Z.; Funk, C. D.; Lusis, A. J. *Circ. Res.* **2002**, *91*, 120.

(3) Mehrabian, M.; Allayee, H. *Curr. Opin. Lipidol.* **2003**, *14*, 447.

(4) Helgadottir, A.; Manolescu, A.; Thorleifsson, G.; Gretarsdottir, S.; Jonsdottir, H.; Thorsteinsdottir, U.; Samani, N. J.; Gudmundsson, G.; Grant, S. F. A.; Thorgeirsson, G.; Sveinbjornsdottir, S.; Valdimarsson, E. M.; Matthiasson, S. E.; Johannsson, H.; Gudmundsdottir, O.; Gurney, M. E.; Sainz, J.; Thorhallsdottir, M.; Andresdottir, M.; Frigge, M. L.; Topol, E. J.; Kong, A.; Gudnason, V.; Hakonarson, H.; Gulcher, J. R.; Stefansson, K. *Nat. Genet.* **2004**, *36*, 233.

(5) Jawien, J.; Gajda, M.; Rudling, M.; Mateuszuk, L.; Olszanecki, R.; Guzik, T. J.; Chlopicki, S.; Korbut, R. *Eur. J. Clin. Invest.* **2006**, *36*, 141.

(6) Jawien, J.; Gajda, M.; Olszanecki, R.; Korbut, R. *J. Physiol. Pharmacol.* **2007**, *58*, 583.

(7) Hakonarson, H.; Thorvaldsson, S.; Helgadottir, A.; Gudbjartsson, D.; Zink, F.; Andresdottir, M.; Manolescu, A.; Arnar, D. O.; Andersen, K.; Sigurdsson, A.; Thorgeirsson, G.; Jonsson, A.; Agnarsson, U.; Bjornsdottir, H.; Gottskalksson, G.; Einarsson, A.; Gudmundsdottir, H.; Adalsteinsdottir, A.; Gudmundsson, K.; Kristjansson, K.; Hardarson, T.; Kristinsson, A.; Topol, E. J.; Gulcher, J.; Kong, A.; Gurney, M.; Thorgeirsson, G.; Stefansson, K. *J. Am. Med. Assoc.* **2005**, *293*, 2245.

(8) Funk, C. D. *Nat. Rev. Drug Discov*ery **2005**, *4*, 664.

(9) Evans, J. F.; Ferguson, A. D.; Mosley, R. T.; Hutchinson, J. H. *Trends Pharmacol. Sci.* **2008**, *29*, 72.

(10) Tager, A. M.; Bromley, S. K.; Medoff, B. D.; Islam, S. A.; Bercury, S. D.; Friedrich, E. B.; Carafone, A. D.; Gerszten, R. E.; Luster, A. D. *Nat. Immunol.* **2003**, *4*, 982.

(11) Sjostrom, M.; Johansson, A. S.; Schroder, O.; Qiu, H.; Palmblad, J.; Haeggström, J. Z. *Arterioscler. Thromb. Vasc. Biol.* **2003**, *23*, e37.

(12) Lotzer, K.; Spanbroek, R.; Hildner, M.; Urbach, A.; Heller, R.; Bretschneider, E.; Galczenski, H.; Evans, J. F.; Habenicht, A. J. *Arterioscler. Thromb. Vasc. Biol.* **2003**, *23*, e32.

(13) Spanbroek, R.; Grabner, R.; Lotzer, K.; Hildner, M.; Urbach, A.; Ruhling, K.; Moos, M. P.; Kaiser, B.; Cohnert, T. U.; Wahlers, T.; Zieske, A.; Plenz, G.; Robenek, H.; Salbach, P.; Kuhn, H.; Rådmark, O.; Samuelsson, B.; Habenicht, A. J. *Proc. Natl. Acad. Sci. U.S.A.* **2003**, *100*, 1238.

(14) Aiello, R. J.; Bourassa, P. A.; Lindsey, S.; Weng, W.; Freeman, A.; Showell, H. J. *Arterioscler. Thromb. Vasc. Biol.* **2002**, *22*, 443.

(15) Subbarao, K.; Jala, V. R.; Mathis, S.; Suttles, J.; Zacharias, W.; Ahamed, J.; Ali, H.; Tseng, M. T.; Haribabu, B. *Arterioscler. Thromb. Vasc. Biol.* **2004**, *24*, 369.

(16) Gennaro, A. Di.; Wågsäter, D.; Mäyränpää, M. I.; Gabrielsen, A.; Swedenborg, J.; Hamsten, A.; Samuelsson, B.; Eriksson, P.; Haeggström, J. Z. *Proc. Natl. Acad. Sci. U.S.A.* **2010**, *107*, 21093.