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Supplementary material

Title:

Tailor-made inflammation: how neutrophil serine proteases modulate the inflammatory response

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Supplementary Table 1

	Influence on inflammation	Substrate	Cleavage site	Modification	Experiment	References
PR3	Pro-inflammatory	CXCL8	PRSA↓K_8ELR	Truncation	In vitro, cell based	(1;2)
		Annexin		Degradation	In vitro, cell based	(3)
		CAP18	KRFA↓L_{134}LGD	Activation	Ex vivo	(4-6)
		Il-1β		Activation	In vitro, cell based	(7)
		Il-18		Activation	In vitro, cell based	(8)
		Il-32	HLET↓VAAY	Activation	In vitro	(9-11)
		TNFα	AQAV↓R_{78}SSS	Activation	Ex vivo	(12-15)
	Anti-inflammatory	CCL3(L1)		Degradation	In vitro, cell based	(16)
		Chemerin	GQFA↓F_{156}SKA	Inactivation	In vitro, cell based	(6;17)
		Il-6	TTNA↓S_{174}LLT	Inactivation	Ex vivo	(18)
NE	Pro-inflammatory	CCL15	ENPV↓V_{22}LNS	Truncation	Ex vivo	(2;19)
		CCL23	FHAT↓S_{30}ADCC	Truncation	Ex vivo	(2;19)
		Chemerin	FAFS↓K_{158}ALP	Inactivation	In vitro, cell based	(6;20;21)
		Granulin		Degradation	In vitro	(2;22)
	Anti-inflammatory	CXCL7		Degradation	In vitro	(2;23)
		CXCL8		Degradation	In vitro	(2;24)
		CXCL12		Degradation	In vitro, cell based	(25)
		CCL3(L1)		Degradation	In vitro, cell based	(2;16)
		CAP18		Degradation	In vitro	(4)
		TNFα		Degradation	In vitro, cell based	(26;27)
		Il-2		Degradation	In vitro	(24)
		Il-6		Degradation	Ex vivo	(18)
CG	Pro-inflammatory	CXCL5	AAVL↓R_9ELR	Truncation	In vitro	(2;28)
		CXCL7	SDLY↓A_{59}ELR	Truncation	In vitro, cell based	(2;29;30)
		CCL15	SFHF↓A_{29}ADCC	Truncation	Ex vivo	(2;19)
		CCL23	LDRF↓H_{27}ATS	Truncation	Ex vivo	(2;19)
		Chemerin	QFAF↓S_{157}KAL	Activation	In vitro, cell based	(6;20;21)
	Anti-inflammatory	CCL3(L1)		Degradation	In vitro, cell based	(16)
		CAP18		Degradation	In vitro	(4)
		Il-6	QSGF↓N_{107}EET	Inactivation	Ex vivo	(18)
		TNFα		Degradation	In vitro, cell based	(26;27)

Reference List

1. Padrines,M., Wolf,M., Walz,A., and Baggiolini,M. 1994. Interleukin-8 processing by neutrophil elastase, cathepsin G and proteinase-3. *FEBS Lett.* 352:231-235.

2. Mortier,A., Van Damme,J., and Proost,P. 2008. Regulation of chemokine activity by posttranslational modification. *Pharmacol.Ther.* 120:197-217.

3. Vong,L., D'Acquisto,F., Pederzoli-Ribeil,M., Lavagno,L., Flower,R.J., Witko-Sarsat,V., and Perretti,M. 2007. Annexin 1 cleavage in activated neutrophils: a pivotal role for proteinase 3. *J.Biol.Chem.* 282:29998-30004.

4. Sorensen,O.E., Follin,P., Johnsen,A.H., Calafat,J., Tjabringa,G.S., Hiemstra,P.S., and Borregaard,N. 2001. Human cathelicidin, hCAP-18, is processed to the antimicrobial peptide LL-37 by extracellular cleavage with proteinase 3. *Blood* 97:3951-3959.

5. de Haar,S.F., Hiemstra,P.S., van Steenbergen,M.T., Everts,V., and Beertsen,W. 2006. Role of polymorphonuclear leukocyte-derived serine proteinases in defense against Actinobacillus actinomycetemcomitans. *Infect.Immun.* 74:5284-5291.

6. Zabel,B.A., Zuniga,L., Ohyama,T., Allen,S.J., Cichy,J., Handel,T.M., and Butcher,E.C. 2006. Chemoattractants, extracellular proteases, and the integrated host defense response. *Exp.Hematol.* 34:1021-1032.

7. Coeshott,C., Ohnemus,C., Pilyavskaya,A., Ross,S., Wieczorek,M., Kroona,H., Leimer,A.H., and Cheronis,J. 1999. Converting enzyme-independent release of tumor necrosis factor alpha and IL-1beta from a stimulated human monocytic cell line in the presence of activated neutrophils or purified proteinase 3. *Proc.Natl.Acad.Sci.U.S.A* 96:6261-6266.

8. Sugawara,S., Uehara,A., Nochi,T., Yamaguchi,T., Ueda,H., Sugiyama,A., Hanzawa,K., Kumagai,K., Okamura,H., and Takada,H. 2001. Neutrophil proteinase 3-mediated induction of bioactive IL-18 secretion by human oral epithelial cells. *J.Immunol.* 167:6568-6575.

9. Choi,J.D., Bae,S.Y., Hong,J.W., Azam,T., Dinarello,C.A., Her,E., Choi,W.S., Kim,B.K., Lee,C.K., Yoon,D.Y. *et al.* 2009. Identification of the most active interleukin-32 isoform. *Immunology* 126:535-542.

10. Novick,D., Rubinstein,M., Azam,T., Rabinkov,A., Dinarello,C.A., and Kim,S.H. 2006. Proteinase 3 is an IL-32 binding protein. *Proc.Natl.Acad.Sci.U.S.A* 103:3316-3321.

11. Kim,S., Lee,S., Her,E., Bae,S., Choi,J., Hong,J., Jaekal,J., Yoon,D., Azam,T., Dinarello,C.A. *et al.* 2008. Proteinase 3-processed form of the recombinant IL-32 separate domain. *BMB.Rep.* 41:814-819.

12. Robache-Gallea,S., Morand,V., Bruneau,J.M., Schoot,B., Tagat,E., Realo,E., Chouaib,S., and Roman-Roman,S. 1995. In vitro processing of human tumor necrosis factor-alpha. *J.Biol.Chem.* 270:23688-23692.

13. Bank,U. and Ansorge,S. 2001. More than destructive: neutrophil-derived serine proteases in cytokine bioactivity control. *J.Leukoc.Biol.* 69:197-206.

14. Armstrong,L., Godinho,S.I., Uppington,K.M., Whittington,H.A., and Millar,A.B. 2006. Contribution of TNF-alpha converting enzyme and proteinase-3 to TNF-alpha processing in human alveolar macrophages. *Am.J.Respir.Cell Mol.Biol.* 34:219-225.

15. Armstrong,L., Godinho,S.I., Uppington,K.M., Whittington,H.A., and Millar,A.B. 2009. Tumour necrosis factor-alpha processing in interstitial lung disease: a potential role for exogenous proteinase-3. *Clin.Exp.Immunol.* 156:336-343.

16. Ryu,O.H., Choi,S.J., Firatli,E., Choi,S.W., Hart,P.S., Shen,R.F., Wang,G., Wu,W.W., and Hart,T.C. 2005. Proteolysis of macrophage inflammatory protein-1alpha isoforms LD78beta and LD78alpha by neutrophil-derived serine proteases. *J.Biol.Chem.* 280:17415-17421.

17. Guillabert,A., Wittamer,V., Bondue,B., Godot,V., Imbault,V., Parmentier,M., and Communi,D. 2008. Role of neutrophil proteinase 3 and mast cell chymase in chemerin proteolytic regulation. *J.Leukoc.Biol.* 84:1530-1538.

18. Bank,U., Kupper,B., Reinhold,D., Hoffmann,T., and Ansorge,S. 1999. Evidence for a crucial role of neutrophil-derived serine proteases in the inactivation of interleukin-6 at sites of inflammation. *FEBS Lett.* 461:235-240.

19. Berahovich,R.D., Miao,Z., Wang,Y., Premack,B., Howard,M.C., and Schall,T.J. 2005. Proteolytic activation of alternative CCR1 ligands in inflammation. *J.Immunol.* 174:7341-7351.

20. Wittamer,V., Bondue,B., Guillabert,A., Vassart,G., Parmentier,M., and Communi,D. 2005. Neutrophil-mediated maturation of chemerin: a link between innate and adaptive immunity. *J.Immunol.* 175:487-493.

21. Zabel,B.A., Allen,S.J., Kulig,P., Allen,J.A., Cichy,J., Handel,T.M., and Butcher,E.C. 2005. Chemerin activation by serine proteases of the coagulation, fibrinolytic, and inflammatory cascades. *J.Biol.Chem.* 280:34661-34666.

22. Zhu,J., Nathan,C., Jin,W., Sim,D., Ashcroft,G.S., Wahl,S.M., Lacomis,L., Erdjument-Bromage,H., Tempst,P., Wright,C.D. *et al.* 2002. Conversion of proepithelin to epithelins: roles of SLPI and elastase in host defense and wound repair. *Cell* 111:867-878.

23. Cohen,A.B., Stevens,M.D., Miller,E.J., Atkinson,M.A., and Mullenbach,G. 1992. Generation of the neutrophil-activating peptide-2 by cathepsin G and cathepsin G-treated human platelets. *Am.J.Physiol* 263:L249-L256.

24. Leavell,K.J., Peterson,M.W., and Gross,T.J. 1997. Human neutrophil elastase abolishes interleukin-8 chemotactic activity. *J.Leukoc.Biol.* 61:361-366.

25. Padrines, M., et al., *Interleukin-8 processing by neutrophil elastase, cathepsin G and proteinase-3.* FEBS Lett, 1994. 352(2): p. 231-5.

26. Scuderi,P., Nez,P.A., Duerr,M.L., Wong,B.J., and Valdez,C.M. 1991. Cathepsin-G and leukocyte elastase inactivate human tumor necrosis factor and lymphotoxin. *Cell Immunol.* 135:299-313.

27. van Kessel,K.P., van Strijp,J.A., and Verhoef,J. 1991. Inactivation of recombinant human tumor necrosis factor-alpha by proteolytic enzymes released from stimulated human neutrophils. *J.Immunol.* 147:3862-3868.

28. Nufer,O., Corbett,M., and Walz,A. 1999. Amino-terminal processing of chemokine ENA-78 regulates biological activity. *Biochemistry* 38:636-642.

29. Brandt,E., Van Damme,J., and Flad,H.D. 1991. Neutrophils can generate their activator neutrophil-activating peptide 2 by proteolytic cleavage of platelet-derived connective tissue-activating peptide III. *Cytokine* 3:311-321.

30. Ehlert,J.E., Ludwig,A., Grimm,T.A., Lindner,B., Flad,H.D., and Brandt,E. 2000. Down-regulation of neutrophil functions by the ELR(+) CXC chemokine platelet basic protein. *Blood* 96:2965-2972.