Properdin, the Positive Regulator of Complement, Is Highly C-Mannosylated

Steffen Hartmann and Jan Hofsteenge†
From the Friedrich-Miescher Institut, CH-4058 Basel, Switzerland

Properdin is the positive regulator of the alternative pathway of complement activation. The 53-kDa protein is essentially composed of six thrombospondin type 1 repeats, all of which contain the WXXW motif, the recognition sequence for C-mannosylation. C-Mannosylation is a post-translational modification of tryptophan residues in which, in contrast to the well known N- and O-glycosylation, the carbohydrate is attached via a C–C bond to the C-2 of the indole ring of tryptophan. C-Mannosylation was first found in human RNase 2 and interleukin-12. The terminal complement proteins C6–C9 also carry this modification as part of their thrombospondin type 1 repeats. We studied the C-mannosylation pattern of human properdin by mass spectrometry and Edman degradation. Properdin contains 20 tryptophans of which 17 are part of a WXXW motif. Fourteen tryptophans were found to be modified 100%. This is the first example of a protein in which the majority of tryptophan residues occurs in the C-mannosylated form. These results show that C-mannosylated proteins occur at several steps along the complement activation cascade. Therefore, this system would be ideal to investigate the function of C-mannosylation.

Glycosylation is one of the most abundant and widespread post-translational modifications of proteins. In the common cases of N- and O-glycosylation the glycan is attached via an amide or a hydroxyl group of an amino acid side chain to the protein. In human RNase 2 a fundamentally different type of glycosylation was discovered (1–3). An α-mannosyl residue was found to be linked via a C–C bond to the C-2 of the indole ring of tryptophan (Fig. 1). It was shown that this modification is enzyme-catalyzed and that dolichylphosphate mannose is the sugar donor (4). In RNase 2 the recognition signal for the transferase was determined to be WXX (or less efficiently WXXF), in which the first tryptophan becomes modified (5). Meanwhile a total of 22 tryptophans in 7 proteins have been shown to be C-mannosylated, i.e. RNase 2 (1), interleukin-12 (6), and terminal complement proteins C6, C7, C8α and β, and C9 (7). The terminal complement proteins showed a more complex pattern of C-mannosylated tryptophans than RNase 2 and interleukin-12. They contain as a part of their thrombospondin repeats (TSRs)1 WXXWXXW motifs, in which both of the first two tryptophans and, surprisingly, also the last one can be C-mannosylated. In addition, in TSRs of C6 and C7, tryptophans were found to be modified although they were not even part of a WXXW motif (7).

The complement system is an innate first line host defense mechanism against microbes. Its activation pathways are composed of three proteolytic cascades, which merge at the cleavage step of (inactive) C3, converting it into active C3b (Fig. 2; reviewed in Ref. 8). Properdin (or factor P) is a positive regulator of the complement system. It stabilizes the C3 convertase (C3bBb) in the feedback loop of the alternative pathway (Fig. 2), protecting it from rapid inactivation (9–11). In addition, the C5 convertase (C3bBbC3b), which converts C5 into C5b, can also bind properdin. This eventually leads to the formation of the membrane attack complex, the actual lytic moiety of complement that will kill the attacked microbe. The importance of properdin is demonstrated in properdin-deficient individuals. These patients have a higher susceptibility to meningococcal infections by Neisseria, leading to fulminant meningitis with mortality rates as high as 75% (reviewed in Ref. 12).

Mature properdin monomer is a 53-kDa protein that occurs in plasma at a specific ratio of dimers, trimers, and tetramers of 26:54:20 (13) and a concentration of 15–25 mg/liter. It consists of six TSRs, which are enclosed by N- and C-terminal parts (14) that show no homology to other proteins. Five of the TSRs contain a WXXWXXWXXC motif, but in the fourth repeat the last tryptophan has been replaced by a valine. One N-glycosylation site is found in the sixth TSR, which is not essential for activity of the protein (15, 16).

Finding C-mannosylation in the TSRs of the terminal complement proteins prompted the question of whether properdin, being composed mainly of TSRs, is also C-mannosylated. In this paper we show that properdin is the first protein in which the majority of tryptophans occurs in the C-mannosylated form. This, together with its clearly defined biological function, makes properdin an ideal protein for functional studies on C-mannosylation.

EXPERIMENTAL PROCEDURES

Materials—Human properdin was purchased from Advanced Research Technologies (San Diego, CA). N-(iodoethyl)trifluoroacetamide was from Sigma. Endoproteinase Lys-C (Achromobacter) was from Wako BioProducts (Richmond, VA).

Protein Chemistry—Properdin was reduced and aminoethylated according to Ref. 17. In brief, 50 μg of properdin were dissolved in 50 μl of 0.5 M Tris-HCl, 6 μM guanidine HCl, 10 mM EDTA and reduced with 0.56 μmol of dithiothreitol for 4 h at room temperature under argon. After adding 1/10 volume of methanol, the solution was heated at 50 °C. 3.1 μl of 4.5 M N-(iodoethyl)trifluoroacetamide dissolved in methanol were added twice and incubated at 50 °C for 60 min and 90 min, respectively. Removal of the trifluoroacetyl protection group was achieved by adding 40 μmol of acetic acid and incubating for 60 min at

electrospray ionization mass spectrometry; ESIMS, electrospray ionization tandem mass spectrometry; PTH-, phenylthiohydantoin; cae, aminoethylated cysteine.

* The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.
† To whom correspondence should be addressed: Friedrich-Miescher Institut, Maulbeerstr. 66, CH-4058 Basel, Switzerland. Tel.: 41-61-697-4531; Fax: 41-61-697-3976; E-mail: Jan.Hofsteenge@fmi.ch.
‡ The abbreviations used are: TSR, thrombospondin type 1 repeat; LC-ESIMS, high performance liquid chromatography interfaced with electron spray ionization mass spectrometry; ESIMS, electrospray ionization tandem mass spectrometry; PTH-, phenylthiohydantoin; cae, aminoethylated cysteine.
C-Mannosylation of Properdin

RESULTS

To obtain peptides from properdin that were suitable for analysis, we took advantage of the spacing of the cysteine residues of its TSRs by aminomethylolation and endoproteinase Lys-C digestion. This yielded peptides ranging from 12 to 21 residues in length. Fractionation of an endoproteinase Lys-C digest of reduced and aminomethylolated properdin was achieved by reversed phase LC-ESIMS (Fig. 3). The mass spectrometry data were extracted for the masses of the expected peptides containing tryptophan(s) without and with one, two, or three hexosyl residue(s), which corresponds to an additional mass of 162 Da per hexosyl residue. The fractions were analyzed by ESIMS and Edman degradation.

**Peptide K52 from the Sixth TSR (TSR 6)—** A peptide with a mass of 1928 Da was found to elute at 35.1 min, corresponding to peptide K52 (residues 353–364) with all three tryptophans C-mannosylated. In the same fraction a second peptide with a mass of 1149 Da was observed, which was identified by ESIMS as peptide K5 (GLLGGVSVEQc). ESIMS of the doubly charged ion of peptide K52 with an m/z value of 965 gave the spectrum shown in Fig. 4. Three times the parent ion [M + 2H]^{2+} showed the loss of 120 Da (corresponding to an m/z value of 60 in the case of a doubly charged ion; indicated with dotted lines in Fig. 4). This loss of 120 Da is characteristic for aromatic C-glycosides (21, 22) and has been instrumental in determining the presence of (C-2-Man-)Trp in several proteins (1, 6, 7). Moreover, multiple water losses can be seen (labeled #), which together with the 120-Da loss, form the fingerprint for a C-linked hexosyl residue. A nearly complete series of y ions together with several b ions confirmed the identity of peptide K52. For all y ions and for some b ions containing a C-mannosylated tryptophan, at least one loss of 120 Da (indicated with dashed lines), often together with the multiple water losses, was observed. This has been illustrated in Fig. 4. Edman degradation of this peptide confirmed that all tryptophans were C-mannosylated. Cycles 3, 6, and 9 of peptide K52 showed a PTH-derivative that comigrated with (C-2-Man-)Trp from RNase 2. No signal for the PTH-derivative of unmodified tryptophan was observed. The C-mannosylation pattern of this peptide is another example of the modification of the last tryptophan in a WXXWWXXX context, as it was first found in the terminal complement proteins (7). These results have been summarized in Table I.

**Peptide K10 from TSR 1—** At 40.3 min a peptide with a mass of 2099 Da was found that was 324 Da heavier than expected from the cDNA sequence for residues 49–66 (14, 23), corresponding to a modification with two hexosyl moieties. The pure peptide was directly analyzed by ESIMS and Edman degradation. The tandem mass spectrum of the doubly charged peptide twice showed a loss of 120 Da from the parent ion. Furthermore, a nearly complete series of b ions was observed, and all of the b ions containing a C-mannosylated tryptophan showed the 120-Da loss (Table I). Interestingly, the spectrum also showed a series of a ions, again with all possible 120-Da losses (data not shown). This experiment allowed us to localize the modified tryptophan to position 56 and 59 (Table I). The assignment was confirmed by Edman degradation.

**Peptide K17–18 from TSR 2—** At 34.8 min a peptide with a mass of 2352 Da was found. This mass fitted to peptide K17–18 (residues 106–121), with an N-terminally aminomethylolated cysteine and all three tryptophans C-mannosylated. The series of b and y ions observed in the ESIMS spectrum, the triple loss of 120 Da from the parent ion, and Edman degradation of the
pure peptide confirmed this (Table I).

**Peptide K26–27 from TSR 3**—A peptide with a mass of 2753 Da was found at 37.7 min that corresponded to the combination peptide K26–27 (residues 158–178) with two hexosyl residues. Apparently, endoproteinase Lys-C had not cleaved the (aminoethyl)Cys–Pro bond at position 163–164. ESIMSMS analysis showed two 120-Da losses from the parent ion. A series of b and y ions confirmed the identity of the peptide and localized the two modified tryptophans to positions 169 and 172 and one unmodified tryptophan to position 175. Edman degradation showed the same pattern of modified and unmodified tryptophans (Table I).

**Peptide K37 from TSR 4**—In the case of peptide K37, endoproteinase Lys-C in the presence of guanidine HCl did not cleave the (aminoethyl)Cys–Pro bond at position 227–228 and 242–243. This resulted in the combination peptide K36–38 (eluting at 36.6 min), which was too large for analysis by ESIMSMS and Edman degradation. To obtain peptide K37, the peptide K36–38 was subjected to a Lys-C digest, but now without guanidine HCl. Its mass of 1834 Da matched that of peptide K37 (residues 228–242) modified with two hexosyl residues. The peptide was purified to apparent homogeneity by LC-ESIMS using a pH 6 buffer system (data not shown). The ESIMSMS spectrum showed two 120-Da losses from the parent ion and a complete y ion series with nearly all possible (C-2-Man-)Trp-related 120-Da losses. Edman degradation confirmed that both tryptophans are C-mannosylated (Table I).

**Peptide K43 from TSR 5**—The sequence of interest was found in two different Lys-C cleavage products: the fully cleaved peptide K43 (at 36.9 min) and the combination peptide K42–43 (at 38.3 min). In both cases the masses were 324 Da heavier than predicted from the cDNA sequence, suggesting the presence of two hexosyl residues (Table I). The ESIMSMS spectra of both peptides showed two characteristic 120-Da losses from the parent ions. Both spectra allowed the assignment of the (C-2-Man-)Trp-related 120-Da losses. Edman degradation showed the same pattern of modified and unmodified tryptophans (Table I).

**DISCUSSION**

The results presented in this paper (Fig. 5) show that 14 of 20 tryptophans in properdin are stoichiometrically C-mannosylated. These tryptophans were identified by tandem mass spectrometry experiments and confirmed by Edman degradation (Table I). Mass spectrometry experiments cannot distinguish...
between different hexoses but enable the establishment of the presence of a C–C bond between the hexosyl residue and tryptophan by observing the 120-Da loss, typical for aromatic C–glycosides (21, 22). Therefore, it was verified by Edman degradation that all PTH-derivatives of modified tryptophans comigrated with authentic PTH-(C-2-Man-)Trp (Table I). For three proteins, RNase 2 (2, 3), interleukin-12 (6), and C9 (7), NMR always identified the hexosyl group to be α-mannose, C-glycosidically linked to the C-2 of the indole moiety. Importantly, the NMR data showed that in C9 this is true for both tryptophans in the WXXW motif (7). Up to now no C-o-hexosylated tryptophan derivatives other than the mannosylated one have been detected; nor are synthetic compounds available. The recent synthesis of (C-2-Man-)Trp should also allow the production of other hexosyl derivatives, which would provide suitable controls (24, 25).

So far seven polypeptides have been shown to contain a total of 22 C-mannosylated tryptophans. Properdin increases this number substantially, further supporting the notion that C-mannosylation is not a rare post-translational modification (7). In the case of RNase 2 (4, 5) and interleukin-12 (6) it has been well established that WXXW is the recognition signal for C-mannosylation, where only the first tryptophan becomes modified. In properdin, only the C-mannosylation of TSR 3 follows this rule (Fig. 5). In the other TSRs, tryptophans occur that are not followed by a second tryptophan (or another aromatic residue) at position +3. Most of the time a cysteine is found at this position; however, in TSR 4 a valine is present. C-Mannosylation of tryptophan residues in such a context has also been observed in the terminal components of complement. This led to the hypothesis that in addition to the WXXW motif, another signal must exist in these proteins (7). At present, it is not

### TABLE I

| Peptide | Residue | Mass | Number of hexoses | Position of modified Trp | MSMS | Retention time of C-mannosylated tryptophan PTH-derivative |
|---------|---------|------|-------------------|--------------------------|------|----------------------------------------------------------|
|         |         | Expected | Observed |                 |                  | Sample | RNase2 |
|         |         |         |         |                  |                  |        |        |
| K10     | 49-66   | 1776    | 2099    | 2                | 56              | 17.21  | 17.19  |
|         |         | 59      |         |                  |                  | 17.24  |        |
| K17-18  | 106-121 | 1865    | 2352    | 3                | 112             | 17.26  | 17.25  |
|         |         |         |         |                  |                  | 17.29  |        |
| K26-27  | 158-178 | 2429    | 2753    | 2                | 169             | 17.24  | 17.19  |
|         |         |         |         |                  |                  | 17.27  |        |
| K37     | 228-242 | 1510    | 1834    | 2                | 233             | 16.42  | 16.42  |
|         |         |         |         |                  |                  | 16.46  |        |
| K43     | 286-300 | 1793    | 2117    | 2                | 294             | 17.18  | 17.17  |
|         |         |         |         |                  |                  | 17.19  |        |
| K52     | 353-364 | 1441    | 1928    | 3                | 355             | 17.37  | 17.25  |
|         |         |         |         |                  |                  | 17.32  |        |
|         |         |         |         |                  |                  | 17.30  |        |

*Peptides from an endoproteinase Lys-C digest have been numbered according to their occurrence in the polypeptide chain.

Residue numbers are according to the mature protein.

Expected mass deduced from the cDNA sequence with aminoethylated cysteines.

Number of expected hexoses: (observed mass – expected mass)/162 Da.

Summary of spectra obtained from differently charged precursor ions. y and b ions that were observed are indicated with a line above and below the peptide sequence, respectively. Ions from which the 120-Da loss (which defines the presence of the C-mannose linkage) has been observed are indicated with a number that reflects the number of times a 120-Da loss occurred. W*, (C-2-Man-)Trp. Cysteines were aminoethylated.

**Fig. 5. Summary of the C-mannosylation pattern of human properdin.**

The amino acids are numbered as they occur in the mature polypeptide chain. Hatched boxes indicate the TSRs. C-mannosyl residues are shown as hexagons.
known what constitutes such a signal. In vitro experiments using synthetic substrates strongly suggest that the additional signal is not formed by the residue at the +3 position (7). If this signal were solely encoded in the primary structure, the signal would lie outside the amino acid sequence used in these studies, and a second kind of C-mannosyltransferase would be involved (7). Alternatively, the signal could be formed by a three-dimensional signal patch, as has been described for substrates of UDP-GlcNAc lysosomal enzyme:GlcNAc-1-phosphotransferase (26). In TSRs 1 and 5 of properdin the first tryptophan is not C-mannosylated, indicating that negative signals must exist. This could be either beingnombre amino acids or three-dimensional constraints.

The high degree of C-mannosylation of properdin poses the question of degradation of (C-2-Man-)-Trp. On the one hand, pathways could exist that degrade (C-2-Man-)-Trp to intermediates suitable for entering metabolic pathways. On the other hand, (C-2-Man-)-Trp could be excreted, either as part of a peptide or as free (C-2-Man-)-Trp. The latter pathway is compatible with the recent finding of (C-2-Man-)-Trp in human urine (27). Considering the number of C-mannosylated tryptophans in properdin and the terminal complement proteins (7), and the concentrations of these proteins in plasma, the amounts of (C-2-Man-)-Trp found in urine could be readily explained by turnover of only 5% of these proteins per day.

In addition to thrombospondin-1, properdin, and the terminal complement proteins, TSR modules occur in F-, M-, and SCO-spondin (28–31); semaphorin 5A and 5B (32); brain-spondin (28–31); semaphorin 5A and 5B (32); brain-spondin (28–31); semaphorin 5A and 5B (32); 

In conclusion, it has been shown here that human properdin is a highly C-mannosylated protein. The fact that, in addition to the terminal components C6-C9, the positive regulator properdin (with its well-defined biological role) is C-mannosylated makes complement an integral system to investigate the function of this post-translational modification.

Acknowledgments—We thank Renee Matthis for amino acid sequencing, Dr. Daniel Hess for advice throughout the project, and Drs. Jack Bohrer and Daniel Hess for reading the manuscript. We also thank Dr. K. B. Reid (Oxford) for the initial gift of properdin.

REFERENCES

1. Hofsteenge, J., Muller, D. R., de Beer, T., Loffler, A., Richter, W. J., and Vliegenthart, J. F. G. (1994) Biochemistry 33, 13524–13530
2. de Beer, T., Vliegenthart, J. F. G., Loffler, A., and Hofsteenge, J. (1995) Biochemistry 34, 11785–11789
3. Loffler, A., Doucey, M. A., Jansson, A. M., Muller, D. R., de Beer, T., Hess, D., Muelly, M., Richter, W. J., Vliegenthart, J. F. G., and Hofsteenge, J. (1996) Biochemistry 35, 12005–12014
4. Doucey, M. A., Hess, D., Cacan, R., and Hofsteenge, J. (1998) Mol. Biol. Cell 9, 301–309
5. Krieg, J., Hartmann, S., Vicentini, A., Glinsch, W., Hess, D., and Hofsteenge, J. (1998) Mol. Biol. Cell 9, 301–309
6. Doucey, M. A., Hess, D., Blommers, M. J., and Hofsteenge, J. (1999) Glycoconjug. J. 9, 435–441
7. Hofsteenge, J., Blommers, M. H., Hess, D., Furmanek, A., and Miroshnichenko, O. (1999) J. Biol. Chem. 274, 32786–32794
8. Prodinger, W. M., Wurzer, S., and Hierich, M. P. (1999) in Fundamental Immunology (Paul, W. E., ed) 4th Ed., pp. 976–935, Lippincott-Raven Publishers, Philadelphia
9. Fearon, D. T., and Austen, K. F. (1975) J. Exp. Med. 142, 856–863
10. DiScipio, R. G. (1981) Rev. Immunol. 118, 189–191
11. Pangburn, M. K. (1989) Immunol. 142, 202–207
12. Nolan, K. F., Schwabe, W., Kaluz, S., Dierich, M. P., and Reid, K. B. (1991) Eur. J. Immunol. 21, 771–776
13. Farries, T. C., Laehmann, P. J., and Harrison, R. A. (1988) Biochem. J. 252, 51–54
14. Nolan, K. F., Kaluz, S., Higgins, J. M., Goundis, D., and Reid, K. B. (1991) Biochem. J. 287, 291–297
15. Nishikawa, T., Ishikawa, K., and Isobe, M. (1998) Synlett 1, 123–125
16. Vliegenthart, J. F. G., and Hofsteenge, J. (1997) J. Biol. Chem. 272, 26687–26692
17. Willems, M., and Mann, M. (1996) Anal. Chem. 68, 1–8
18. Pisano, A., Redmond, J. W., Williams, K. L., and Gooley, A. A. (1993) Glycobiology 3, 429–435
19. Li, Q. M., and van de Heurik, H., Dille, L., and Claey s, M. (1992) Bio ma. Mass. Spectrom. 21, 213–221
20. Becchi, M., and Fraise, D. (1989) Biomed. Environ. Mass Spectrom. 18, 123–130
21. Nolan, K. F., Kaluz, S., Higgins, J. M., Goundis, D., and Reid, K. B. (1991) Biochem. J. 276, 957–970
22. Shibata, S., Ito, Y. (1999) J. Biol. Chem. 274, 9574–9575
23. Baranski, T. J., Koelsch, G., Hartsuck, J. A., and Kornfeld, S. (1991) J. Biol. Chem. 266, 23385–23372
24. Gutsche, B., Grun, C., Schuetzow, D., and Herderich, M. (1999) Biochem. J. 343, 11–19
25. Umemiya, T., Takeuchi, M., and Noda, A. (1997) Dev. Biol. 186, 165–176
26. Gobron, S., Monnerie, H., Meiniel, A., Creveaux, I., Lehmann, W., Lamalle, D., Dastugue, B., and Meiniel, A. (1996) J. Cell Sci. 109, 1053–1061
27. Adams, R. H., Betz, H., and Puschel, A. W. (1996) Mech. Dev. 57, 33–45
28. Nishimori, H., Shiratsuchi, T., Urano, T., Kimura, Y., Kiyono, K., Tatsumi, K., Yoshiba, K., Ono, M., Kawano, M., Nakam y, T., and Tokino, T. (1997) Oncogene 16, 2145–2151
29. Shiratsuchi, T., Nishimori, H., Ichise, H., Nakam y, T., and Tokino, T. (1997) Cytogenet. Cell Genet. 79, 103–108
30. Kurosaki, T., Kanda, N., Ioka, M., Fujiki, F., Ichimura, F., and Matsu saka, M. (1997) J. Biol. Chem. 272, 556–562
31. Tortorella, M. D., Pratta, M. A., Abbaszade, I., Hollis, J. L., Solomon, K., George, H., Bruckner, R., Nagase, H., Itoh, Y., Ellis, D. M., Ross, H., Wiswall, B. H., Murphy, K., Hillman, M. C., Jr., Hollis, J. L., Glinsch, W., Newton, B. C., Magolda, R. L., Trazanos, J. M., and Arner, E. C. (1999) Science 285, 119–122
32. Abbaszade, I., Liu, R. Q., Yang, F., Feinstein, S. A., Ross, O. H., Link, J., Ellis, D. M., Tortorella, M. D., Pratta, M. A., Hollis, J. M., Wynn, R., Duke, J. L., George, H. J., Hillman, M. C., Jr., Murphy, K., Wiswall, B. H., Copeland, R. A., Decicco, C. P., Bruckner, R., Nagase, H., Itoh, Y., Newton, B. C., Magolda, R. L., Trazanos, J. M., Hollis, G. F., Arner, E. C., and Burn, T. C. (1999) J. Biol. Chem. 274, 23443–23445
33. Hurskainen, T. L., Hirohata, S., Seldin, M. F., and Apte, S. S. (1999) J. Biol. Chem. 274, 25555–25563
34. Tang, B. L., and Hong, W. (1999) FEBS Lett. 445, 223–225
35. Bieleloch, R., and Kimble, J. (1999) Nature 398, 586–590

Downloaded from http://www.jbc.org/ by guest on July 23, 2018
C-Mannosylation of Properdin

41. Leung-Hagesteijn, C., Spence, A. M., Stern, B. D., Zhou, Y., Su, M.-W., Hegecock, E. W., and Culotti, J. G. (1992) Cell 71, 289–299
42. Colige, A., Li, S. W., Sieron, A. L., Nussenz, B. V., Prockop, D. J., and Lapierre, C. M. (1997) Proc. Natl. Acad. Sci. U. S. A. 94, 2374–2379
43. Nardi, J. B., Martos, R., Walden, K. K., Lampe, D. J., and Robertson, H. M. (1999) Insect Biochem. Mol. Biol. 29, 883–897
44. Robson, K. J. H., Hall, J. R. S., Jennings, M. W., Harris, T. J. R., Marsh, K., Newbold, C. I., Tate, V. E., and Weatherall, D. J. (1988) Nature 335, 79–82
45. Prater, C. A., Plotkin, J., Jaye, D., and Frazier, W. A. (1991) J. Cell Biol. 112, 1031–1040
46. Sipes, J. M., Krutzsch, H. C., Lawler, J., and Roberts, D. D. (1999) J. Biol. Chem. 274, 22755–22762
47. Li, W.-X., Howard, R. J., and Leung, L. K. L. (1993) J. Biol. Chem. 268, 16179–16184
48. Dawson, D. W., Pearce, F. A., Yhong, R., Silverstein, R. L., and Frazier, W. A. (1997) J. Cell Biol. 138, 707–717
49. Crombie, R. R., Silverstein, R. L., MacLow, C., Pearce, S. F. A., Nachman, R. L., and Laurence, J. (1998) J. Exp. Med. 187, 25–35
50. Guo, N., Krutzsch, H. C., Negre, E., Vogel, T., Blake, D. A., and Roberts, D. D. (1992) Proc. Natl. Acad. Sci. U. S. A. 89, 3040–3044
51. Lambris, J. D., Alsenz, J., Schulz, T. F., and Dierich, M. P. (1984) Biochem. J. 217, 323–326
52. Daoudaki, M. E., Becherer, J. D., and Lambris, J. D. (1988) J. Immunol. 140, 1577–1580
53. Farries, T. C., Lauchmann, P. J., and Harrison, R. A. (1988) Biochem. J. 253, 667–673
54. Holt, G. D., Pangburn, M. K., and Ginsburg, V. (1990) J. Biol. Chem. 265, 2852–2855
55. Stankowski, S., Wey, J., Kalb, E., and Goundis, D. (1991) Biochim. Biophys. Acta 1068, 61–67
56. Sharon, N. (1986) in The Lectins: Properties, Functions, and Applications in Biology and Medicine (Liener, I. E., Sharon, N., and Goldstein, I. J., eds) pp. 493–527, Academic Press, Orlando, FL
57. Turner, M. W. (1996) Immunol. Today 17, 532–540
Properdin, the Positive Regulator of Complement, Is Highly C-Mannosylated
Steffen Hartmann and Jan Hofsteenge

J. Biol. Chem. 2000, 275:28569-28574.
doi: 10.1074/jbc.M001732200 originally published online June 30, 2000

Access the most updated version of this article at doi: 10.1074/jbc.M001732200

Alerts:
- When this article is cited
- When a correction for this article is posted

Click here to choose from all of JBC's e-mail alerts

This article cites 55 references, 29 of which can be accessed free at
http://www.jbc.org/content/275/37/28569.full.html#ref-list-1