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(21) International Application Number: PCT/GB98/00848 (22) International Filing Date: 20 March 1998 (20.03.98) (30) Priority Data: 97 05787.1 20 March 1997 (20.03.97) GB (71) Applicant (for all designated States except US): THROMBOSIS RESEARCH INSTITUTE [GB/GB]; Emmanuel Kaye Building, Manresa Road, Chelsea, London SW3 6LR (GB). (72) Inventors; and (75) Inventors/Applicants (for US only): LU, Xijie [GB/GB]; 78 Lambourn Close, Hanwell, London W7 2LN (GB). SCULLY, Michael, Finbarr [GB/GB]; Douglas House, Crays Hill, Essex CM11 2XN (GB). KAKKAR, Vijay, Vir [GB/GB]; Hambles Edge, Brook Avenue, Warsash, Hants SO3 6HN (GB). AUTHI, Kalwant, Singh [GB/GB]; 19 Woodstock Gardens, Goodmayes, Ilford, Essex IG3 9SZ (GB). (74) Agents: BIZLEY, Richard, Edward et al.; Hepworth Lawrence Bryer & Bizley, Merlin House, Falconry Court, Bakers Lane, Epping, Essex CM16 5DQ (GB).	(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>	

(54) Title: BI- OR MULTIFUNCTIONAL MOLECULES BASED ON A DENDROASPIN SCAFFOLD

Sequence alignment of modified dendroaspin

RICTMILGTEPTTET	CGEDSCYKMINITTONILRG	CGCTTPAGDMPGFTCCRSKCNL	
---FTPR-DM-GPTPGP	-----ISRLIDRTMANFL	-----	DEN-RGD1
-----	-----ISRLIDRTMANFL	-----	DEN-PDGF23
---FTPR-DM-GPTPGP	-----ISRLIDRTMANFL	-----	DEN-PDGF23
-----	-----ISRLIDRTMANFL	-----	DEN-PDGF24
---ISRLIDRTMANFL	-----	-----	DEN-PDGF1
---ISRLIDRTMANFL	-----KKIKIVKK-----	-----	DEN-PDGF13
---GDTDLKDYTPEDTE	-----	-----	DEN-GP11
---GCGPFEI-REYL	-----PEP-----	-----	DEN-HR21
---RP-----	---GCGPFEIPEYTP-P	-----	DEN-HR22
-----	---PEGRILEDDG-TEIDE	-----	DEN-TN2
-----	---GDTDLKDYTPEDTE	-----	DEN-GP21
-----	---GDTDLKDYTPEDTEPGP	-----	DEN-GP22
---FTPR-DM-GPTPGP	-----	---FTPRQSDNDGDFEIPENYLQ	DEN-HR11
-----	---FTPRGDMPGFY	---FTPRQSDNDGDFEIPENYLQ	DEN-HR21
-----	-----	---FTPRQSDNDGDFEIPENYLQ	DEN-HR22
---FTPR-DM-GPTPGP	-----	---PGPCEPCECYILDGGFICTDIDE	DEN-TN11
-----	---FTPRGDMPGFY	---PGPCEPCECYILDGGFICTDIDE	DEN-TN21
-----	-----	---PGPCEPCECYILDGGFICTDIDE	DEN-TN22

(57) Abstract

Dendroaspin, a polypeptide neurotoxin analogue is modified by recombinant DNA techniques, particularly "loop grafting" to provide a modified polypeptide. The modified polypeptide is constructed so as to retain dendroaspin activity e.g. platelet adhesion to fibrinogen in addition to possessing one or more further biological or biochemical activities not native to dendroaspin, e.g. platelet derived growth factor (PDGF) activity or hirudin activity.