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(21) International Application Number: PCT/US92/02312 (22) International Filing Date: 20 March 1992 (20.03.92) (30) Priority data: 675,754 27 March 1991 (27.03.91) US (71) Applicant: LANKENAU MEDICAL RESEARCH CENTER [US/US]; 100 Lancaster Avenue, Wynnewood, PA 19096 (US). (72) Inventor: MULLIN, James, M. ; 133 E. Benedict Avenue, Havertown, PA 19083 (US). (74) Agents: DROBILE, James, A. et al.; Schnader, Harrison, Segal & Lewis, Suite 3600, 1600 Market Street, Philadelphia, PA 19103 (US).		(81) Designated States: AT, AT (European patent), AU, BB, BE (European patent), BF (OAPI patent), BG, BJ (OAPI patent), BR, CA, CF (OAPI patent), CG (OAPI patent), CH, CH (European patent), CI (OAPI patent), CM (OAPI patent), CS, DE, DE (European patent), DK, DK (European patent), ES, ES (European patent), FI, FR (European patent), GA (OAPI patent), GB, GB (European patent), GN (OAPI patent), GR (European patent), HU, IT (European patent), JP, KP, KR, LK, LU, LU (European patent), MC (European patent), MG, ML (OAPI patent), MN, MR (OAPI patent), MW, NL, NL (European patent), NO, PL, RO, RU, SD, SE, SE (European patent), SN (OAPI patent), TD (OAPI patent), TG (OAPI patent). 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> (88) Date of publication of the international search report: 12 November 1992 (12.11.92)
(54) Title: METHOD OF ADMINISTERING DRUGS THROUGH MODIFICATION OF EPITHELIAL TIGHT JUNCTIONS BY TUMOR NECROSIS FACTOR (57) Abstract A method and system for paracellularly administering pharmacologically-active substances across mammalian epithelial barriers, comprising sequentially administering to predetermined epithelial cells of said mammalian epithelial cell sheets having receptors for tumor necrosis factor located thereon and having a homeostatic tight junctional resistance therebetween, an amount of a biologically-active substance reactive with said receptors for tumor necrosis factor in an amount effective to lower said homeostatic tight junctional resistance to permit paracellular transit of said pharmacologically-active substances across said epithelial cell sheets; and followed by exogenously administering a pharmacologically-active substance in a pharmaceutically-acceptable carrier to said predetermined mammalian epithelial barrier before said tight junctional resistance reverts to said homeostatic state.		

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