

- [54] **HOMOGENEOUS INTERLEUKIN 1**
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- [58] **Field of Search** **530/351, 412, 530/413, 414, 417**

[56] **References Cited****U.S. PATENT DOCUMENTS**

4,172,091	10/1979	De Maeyer et al.	424/85
4,406,830	9/1983	Fabricius et al.	530/351
4,508,833	4/1985	Sonneborn et al.	530/351
4,546,161	10/1985	Harvey et al.	530/413
4,762,914	8/1988	Auron et al.	530/351
4,766,069	8/1988	Auron et al.	435/240.1
4,770,781	9/1988	Schmidt et al.	530/351
4,774,320	9/1988	Tagliabue et al.	530/351

FOREIGN PATENT DOCUMENTS

0092163 10/1983 European Pat. Off. .

OTHER PUBLICATIONS

- Sofer et al. *BioTechniques* Nov./Dec. 1983 pp. 198-203.
- Dean et al. *J. Chromatography* 165, 1979, pp. 301-319.
- Auron et al. *PNAS* 81, 1984, pp. 7907-7911.
- Windle et al. *J. Immunol* 132, 1984, pp. 1317-1322.
- Mizel, "Interleukin 1 and T Cell Activation", *Immunol. Rev* vol. 63, 1982, pp. 51-72.
- Dye-Ligand Chromatography*, Amicon Corporation (Lexington, Mass.) (1980) (Chapters 1-3).
- March et al., "Cloning, sequence and expression of two distinct human interleukin-1 complementary DNAs," *Nature* 315:641-647 (1985).
- G. Blyden et al., "Purification and Properties of Human Lymphocyte Activating Factor (LAF)," 118 *J. Immunol.* 1631-1638 (1977).
- L. B. Lachman et al., "Partial Purification of Human Lymphocyte-Activating Factor (LAF) By Ultrafiltration and Electrophoretic Techniques," 119 *J. Immunol.* 2019-2023 (1977).

A. Togawa et al., "Characterization of Lymphocyte-Activating Factor (LAF) Produced By Human Mononuclear Cells: Biochemical Relationship of High and Low Molecular Weight Forms of LAF," 122 *J. Immunol.* 2112-2118 (1979).

S. B. Mizel et al., "Characterization of Lymphocyte-Activating Factor (LAF) Produced by a Macrophage Cell Line, P388D₁, II. Biochemical Characterization of LAF Induced by Activated T Cells and LPS," 120 *J. Immunol.* 1504-1508 (1978).

S. B. Mizel et al., "Physicochemical Characterization of Lymphocyte-Activating Factor (LAF)," 122 *J. Immunol.* 2167-2172 (1979).

S. B. Mizel et al., "Purification to Apparent Homogeneity of Murine Interleukin 1," 126 *J. Immunol.* 834-837 (1981).

P. T. Lomedico et al., "Cloning and expression of murine interleukin-1 cDNA in *Escherichia coli*," 312 *Nature* 458-462 (1984).

G. Di Sabato, "Purification and initial characterization of rat interleukin2," 79 *Proc. Natl. Acad. Sci USA* 3020-3023 (1982).

"Minisymposium on Regulation of Connective Tissue Cells by Immune and Inflammatory Cells," *Lymphokine Res.* 1(2):53 (1982).

K. Welte et al., "Purification of Human Interleukin 2 to Apparent Homogeneity and its Molecular Heterogeneity," 156 *J. Exp. Med.*, 454-464 (1982).

O. Acuto, "An Efficient Method for Purification of Human T-Cell Growth Factor," 53 *J. Immunol. Methods* 15-26 (1982).

J. J. Oppenheim et al., "Interleukin 1 is more than an interleukin," *T Lymphocytes Today* 89-95 (1983).

L. B. Lachman, "Human interleukin 1: purification and properties," 42 *Federation Proceedings* 2639-2645 (1983).

A. Kock et al., "Purification of Human Interleukin 1 by High-Performance Liquid Chromatography," 296 *J. Chromat.* 293-300 (1984).

Matsushima et al, *Lymphokine Res.* Oct. 1984 p. 259 (abstract only).

C. A. Dinarello et al., *PNAS* 74:4624, 1977.

K. Welte et al., *J. Exp. Med.* 156:454, 1982.

Mosley, et al. *Proc. Nat'l Acad. Sci. (USA)* 84: 4572, 4576 (1987).

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[57] **ABSTRACT**

Interleukin 1 has been purified by use of various techniques including ion exchange chromatography and dye-ligand affinity chromatography. By these techniques, interleukin 1 has been purified to homogeneity. The high purification of interleukin 1 has enabled the amino acid composition of this protein to be ascertained and its amino acid sequence to be partially determined.

12 Claims, 1 Drawing Sheet