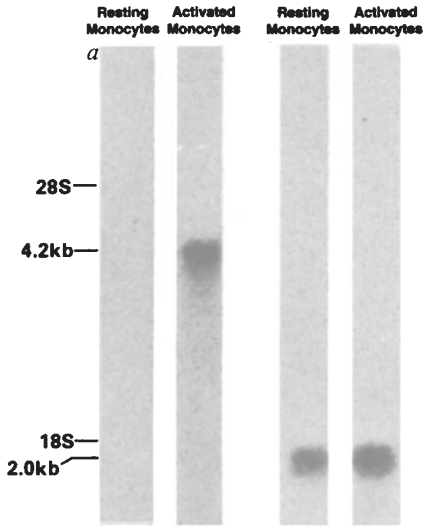

Fig. 3 Expression of the c-*sis* proto-oncogene in human monocytes. *a*, Presence of c-*sis* transcripts in activated monocytes; *b*, presence of γ-actin mRNA transcripts in both resting and activated monocytes.
Methods. Blood monocytes were cultured for 24 h with or without LPS (see Fig. 1*a* legend). After incubation, the cells were washed three times at 4 °C in PBS, *p*H 7.4, collected with a rubber policeman and pelleted by centrifugation (2,000*g*, 5 min). The cell pellet was homogenized in guanidine hydrochloride and subjected to ultracentrifugation through a caesium chloride cushion[41]. Total RNA was enriched for poly(A)$^+$ RNA by one cycle of oligo(dT)-cellulose affinity chromatography[42]. The poly(A)$^+$ RNA (5 μg each lane) samples were subjected to electrophoresis in a 1.1% agarose formaldehyde gel[43] and transferred to a nitrocellulose filter. The filter was hybridized with probes radioactively labelled with ^{32}P by nick-translation[44]. Hybridization and washing conditions were as described by Thomas[45]. RNA sizes were determined by comparison with human (28S, 18S) ribosomal RNA. The c-*sis* probe was clone pL335, a subclone of λ-L33 containing exons 6 and 7 of the human c-*sis* locus[17] kindly provided by E. Gelmann (NCI). The autoradiogram was exposed for 72 h. For *b*, the same filter as in *a* was used. After being allowed to undergo several half-lives of ^{32}P decay of the c-*sis* probe, the filter was hybridized to a human fibroblast cytoplasmic γ-actin cDNA (plasmid pHFγA-1)[46] kindly provided by L. Kedes (Stanford University). The autoradiogram was exposed for 8 h.

c-*sis* proto-oncogene in parallel with the release of a molecule showing PDGF-like activity is of interest in view of the known relationship of c-*sis* to the v-*sis* homologous sequences in the simian sarcoma transforming retrovirus[17], which induces NIH 3T3 fibroblasts and normal rat kidney cells to produce p28$^{v\text{-}sis}$ (ref. 18), a protein of relative molecular mass 28,000 showing close homology to one of the PDGF chains[19–21]. Since PDGF is a growth factor that induces its target cells to enter the G_1 phase of the cell cycle[11], the finding that a transforming virus contains sequences encoding a protein similar to one of the PDGF chains, and that the normal human genome contains sequences with >90% homology with p28$^{v\text{-}sis}$, has important implications for the initial events leading to malignancy. Consistent with these observations, a PDGF-like molecule has been detected in the culture media of human sarcoma[22] and glioma[23] and these cells express c-*sis* mRNA transcripts[24,25].

In addition to implications of the activation of c-*sis* for malignant growth, there is preliminary evidence that this proto-oncogene is involved in normal cell growth. In this context, cultured human and bovine endothelial cells express c-*sis*[26,27] and release a PDGF-like molecule[28], while rat arterial SMC release a PDGF-like protein[29]. Furthermore, using *in situ* hybridization, Goustin *et al.*[30] have recently demonstrated the presence of c-*sis* transcript in the cytotrophoblast of first-trimester human placenta in parallel with the release of a PDGF-like growth activity in the culture media. The present study extends these findings by demonstrating that c-*sis* proto-oncogene expression and release of a PDGF-like molecule occur in the activated human monocyte, a cell of major importance in scar formation and human fibrotic disorders as well as the early development of atherosclerotic plaque. These observations support the theory that common mechanisms are involved in the 'controlled' proliferation of cells involved in normal growth, the 'semi-controlled' proliferation of cells involved in the chronic inflammatory disorders, and the 'uncontrolled' proliferation of malignant cells.

We thank E. Gelmann, G. Wilding, N. Davidson and C. Agnor for help in carrying out this project and la Fondation pour la Recherche Médicale (for Y.M.) and Ministère des Relations Exterieures, France (for J.-F.M.) for partial financial support. *Note added in proof*: Since submission of this manuscript, Shimokado *et al.*[31] have also demonstrated that macrophages express c-*sis* and produce PDGF.

Received 25 July; accepted 18 October 1985.

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Erratum

A closely linked genetic marker for cystic fibrosis

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Nature **318,** 382-384 (1985).

IN this letter, one of the authors' names was omitted (Y.N.). Yusuke Nakamura is at the Howard Hughes Medical Institute.