refractive index along the direction of propagation. In these circumstances, a plane wavefront incident on the medium, at an angle to the direction of modulation, will emerge as a periodically corrugated wavefront resulting in the diffraction of light. Here, for natural light, all the diffraction orders are unpolarized and for polarized light, the state of polarization in all the diffraction orders will be the same as that of the incident light. One other characteristic feature of this diffraction, unlike the diffraction from amplitude gratings, is that the intensity of the orders need not monotonically decrease as one goes to higher orders. In fact, the intensities of the different diffraction orders can wander with the variations in the thickness of the liquid medium or the intensity of the ultrasonic wave. Raman and Nath[3] (RN) were the first to give a satisfactory theory of such a scalar diffraction process. In this model, the internal diffractions are ignored.

In the cholesteric phase grating, the wavefront corrugation is not due to a variation in the mean refractive index but due to a periodic variation in the birefringence. Further, this variation is such that diffraction will occur for linearly polarized light of any azimuth except the one having its azimuth parallel to the twist axis. Another chiral liquid crystal with a comparatively more complicated structure exhibiting diffraction is the chiral smectic C (S_{c^*}). Here the structure consists of a helical stack of layers of uniformly tilted molecules. As one goes from layer to layer, the index ellipsoid spirals about the twist axis at a constant angle, the tilt angle of smectic C. In S_{c^*}, the twist axis is a 1-fold screw axis. This results in extra orders which happen to be the odd orders of the diffraction pattern. In contrast to a cholesteric, in a S_{c^*}, diffraction will occur for incident light of any azimuth.

Recently, Suresh *et al.*[5] reported very unusual polarization and intensity features in diffraction from S_{c^*}. Some of the polarized intensity features associated with this diffraction phenomenon are depicted in Figure 1. The authors find that for any azimuth of the incident light, the diffracted light in all the orders was strongly polarized in the same linear state. Further, depending upon the sample thickness, this linear state was either parallel or perpendicular to the screw axis. These observed intensity and polarization features can be accounted for quite satisfactorily by employing[5] a rigorous theory[6] of diffraction of light in anisotropic dielectric gratings. Unlike RN theory, the rigorous theory incorporates the internal diffractions in the medium. It may be mentioned that in the case of very low birefringence or small sample thicknesses, a generalized RN theory[7] is applicable. In this approximation, the two theories agree and they predict entirely different polarization features. For example, for incident linearly polarized light, the odd orders are always linearly polarized and the even orders are elliptically polarized. Also the intensities of the odd orders are independent of the azimuth of the incident light while it is not true of the even orders. It is interesting to confirm these predictions experimentally.

There are many other examples of phase gratings occurring in a variety of situations. For example, phase grating effects have been studied[8] in a five-fold quasi-crystalline structure formed in water by superimposing five ultrasonic beams arranged according to a regular pentagonal array. Also, in non-linear media, light itself induces refractive index modulations resulting in self-diffraction. It is worthwhile to note that even after six decades, the study of phase gratings continues to be a very active field of research.

1. Sackmann, E., Meiboom, S., Snyder, L. C., Meixner, A. E. and Dietz, R. E., *J. Am. Chem. Soc.*, 1968, **90**, 3567–3570.
2. Ranganath, G. S., *Curr. Sci*, 1972, **41**, 386–391.
3. Raman, C. V. and Nagendra Nath, N. S., *Proc. Indian Acad. Sci.*, 1935, **A2**, 406–412.
4. Debye, P. and Sears, F. W., *Proc. Natl. Acad. Sci.*, 1932, **18**, 409–414.
5. Suresh, K. A., Sah, Yuvaraj, Sunil Kumar, P. B. and Ranganath, G. S., *Phys. Rev. Lett.*, 1994, **72**, 2863–2866.
6. Rokushima, K. and Yamakita, J., *J. Opt. Soc. Am.*, 1983, **73**, 901–908.
7. Suresh, K. A., Sunil Kumar, P. B. and Ranganath, G. S., *Liquid Crystals*, 1992, **11**, 73–82.
8. de Espinosa, F. M., *et al.*, *Europhys. Lett.*, 1993, **21**, 915–920.

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Strategies for regulating nuclear entry of transcription factors

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Selective traffic of macromolecules across the nuclear membrane in a eukaryotic cell affords an additional level of control for the activity of transcription factors. In several instances, the inactive forms of the transcription factors are maintained in the cytoplasm until multiple regulatory influences lead to their activation and transport to the nucleus. However, the details of these regulatory mechanisms are poorly understood in most cases.

In a recent paper from the laboratory of Brown and Goldstein[1], compelling evidence has been presented for a novel strategy of activation which combines a membrane-bound sensor and a transcription factor in one molecule. The molecule in question is the sterol regulatory element binding protein 1 (SREBP-1). SREBP-1 binds to a sequence designated as sterol regulatory element 1 (SRE-1) in the 5′ upstream region of the genes for the low density lipoprotein (LDL) receptor and 3-hydroxy-3-methyl glutaryl CoA synthase, and promotes their transcription when stores of cholesterol and related sterols are low. When cellular sterol levels are replenished, SRE-1 activity is abolished.

SREBP-1 belongs to the basic helix-loop-helix leucine zipper family of transcription factors. Wang *et al*[1] have demonstrated that SREBP-1 is synthesized as a 125 kDa high mole-

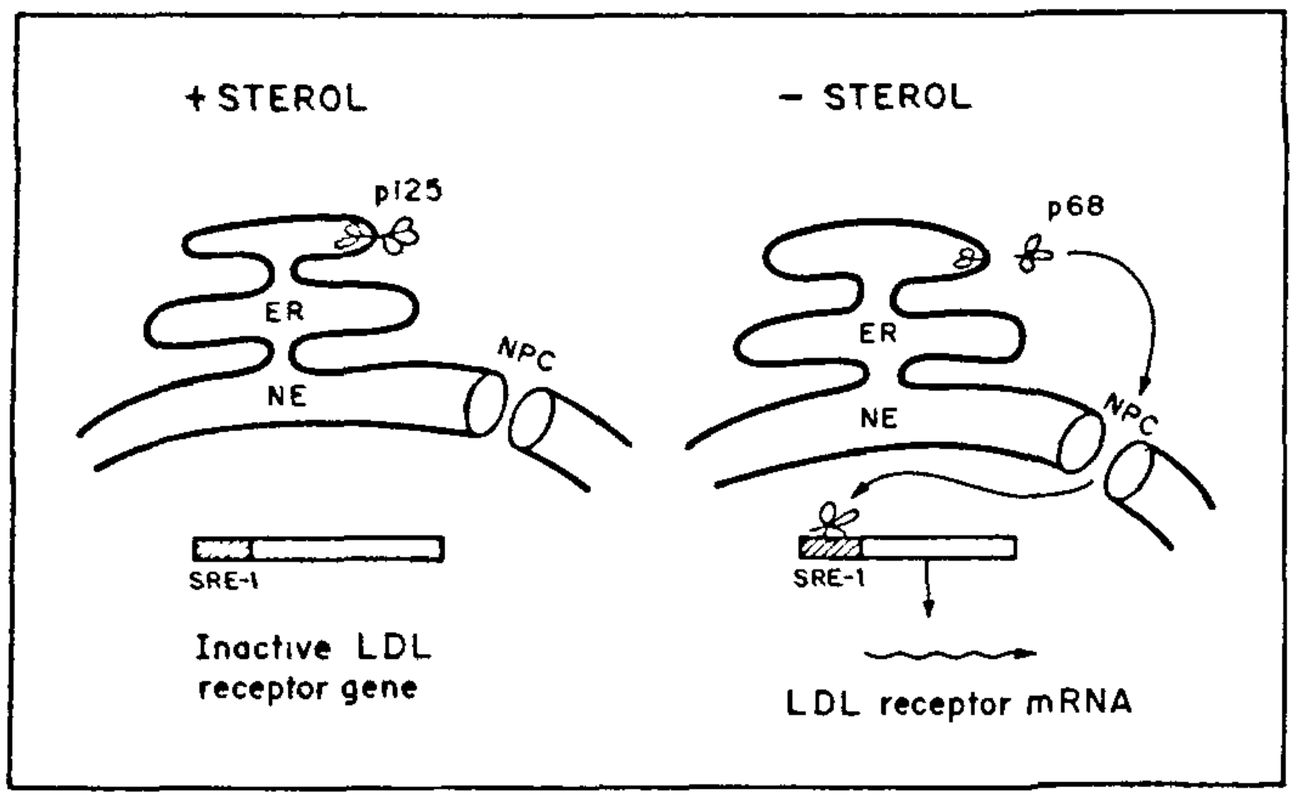

Figure 1. Schematic representation of the conversion of SREBP-1 from the inactive 125 kDa precursor (p 125) to the active 68 kDa form (p 68) in the absence of sterols. ER: endoplasmic reticulum, NE: nuclear envelope, NPC: nuclear pore complex, LDL: low density lipoprotein.

cular mass precursor protein that is bound to the endoplasmic reticulum and the nuclear envelope as an integral membrane protein. When HeLa cells are depleted of sterols, the precursor molecule is cleaved proteolytically to a 68 kDa species that is no longer membrane-bound and can enter the nucleus to stimulate transcription. Addition of sterol to HeLa cells inhibits this conversion but does not affect SREBP-1 mRNA levels, strengthening the view that the regulation of SREBP-1 is primarily posttranslational. The 68 kDa active form contains a nuclear localization signal and the DNA-binding leucine zipper motif to enable it to function in the nucleus.

The predominant mode of activation of steroid hormone receptors is to bind to their respective ligands, translocate into the nucleus and bind to response elements near their target genes. However, this strategy has not been utilized by SREBP-1. One reason for this may be that cholesterol concentration needs to be sensed in the endoplasmic reticulum which is the site of sterol biogenesis, and this signal has to be transmitted to the nucleus to modulate transcription of genes coding for key enzymes. Although the endoplasmic reticulum contains only a fraction of the cholesterol present in the plasma membrane, cholesterol is synthesized in the endoplasmic reticulum and transported through the Golgi apparatus to the plasma membrane. The low content of cholesterol in the endoplasmic reticulum would make it easier to detect small changes in the concentration of free cholesterol here rather than in the cholesterol-rich plasma membrane. It has been speculated that the mechanism for the proteolytic cleavage of the 125 kDa precursor of SREBP-1 to the 68 kDa active form might depend on changes in the properties of the endoplasmic reticulum mediated by cholesterol. An increase in sterol concentration might inhibit proteolytic cleavage by acting on the protease, or by causing a conformational change in the precursor or by increasing the bilayer thickness so as to shield the site of cleavage in the precursor. Thus by combining the properties of a membrane-sensor and transcription factor, SREBP-1 affords a unique approach for relaying a signal from the endoplasmic reticulum to the nucleus.

A second important strategy for control of nuclear translocation is found in the rel family of proteins, which includes the lymphocyte transcription factor NF-κB, the avian oncogene product v-rel and the *Drosophila* morphogen dorsal. NF-κB is present as a complex with its inhibitor IκB in the cytoplasm of uninduced cells, whereas dorsal associates with cactus, a IκB-like protein, in the cytoplasm of early embryos. The proteins IκB and cactus share a motif called the ankyrin repeat which is thought to function in protein–protein interactions and might be involved in anchoring proteins to the cytoskeleton. The mechanism of nuclear targeting of dorsal has been elucidated recently in a report by Whalen and Steward[2]. The dorsal morphogen is known to be localized in the nuclei of cells in the blastoderm stage in a ventral-to-dorsal gradient, with cells in the most ventral nuclei having the highest concentration of dorsal. This selective relocalization of dorsal is positively regulated by the eleven dorsal group gene products in the pathway and negatively controlled by cactus protein. The inactive dorsal–cactus complex is thought to be disrupted by a ventral signal generated by the transmembrane receptor Toll, and transmitted through the cytoplasmic components of the pathway, pelle and tube, resulting in the nuclear localization of dorsal. Whalen and Steward have demonstrated that dorsal and cactus are both phosphoproteins that form a stable complex, mediated by the rel homology region. Although the phosphorylation status of cactus remains relatively constant, dorsal exists as multiply phosphorylated forms that are developmentally regulated. The maximally phosphorylated forms are found in the nuclei. The authors convincingly argue that a series of phosphorylation events mediated by the dorsal group of proteins regulates the nuclear targeting of dorsal.

A role for the phosphorylation of karyophilic proteins at or near their nuclear localization signal sequence has been proposed for the regulated import of simian virus large T antigen, yeast SW15 transcription factor and the nuclear lamins. Phosphorylation of the nuclear transport machinery has been suggested to be necessary for enhanced transport in dividing cells. Future studies may unravel other strategies adopted by the cell to control traffic into the nucleus and thereby influence gene expression.

1. Wang, X., Sato, R., Brown, M S, Hua, X and Goldstein, J L, *Cell*, 1994, 77, 53–62
2. Whalen, A M and Steward, R., *J. Cell Biol*, 1993, **123**, 523–534

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