The *Discussion Forum* provides a medium for airing your views on any issues related to the pharmaceutical industry and obtaining feedback and discussion on these views from others in the field. You can discuss issues that get you hot under the collar, practical problems at the bench, recently published literature, or just something bizarre or humorous that you wish to share. Publication of letters in this section is subject to editorial discretion and company-promotional letters will be rejected immediately. Furthermore, the views provided are those of the authors and are not intended to represent the views of the companies they work for. Moreover, these views do not reflect those of Elsevier, *Drug Discovery Today* or its editorial team. Please submit all letters to Joanna Owens, Acting News & Features Editor, *Drug Discovery Today*, e-mail: Joanna.Owens@elsevier.com

Current understanding of mistletoe lectins ▼

A recent letter in *Drug Discovery Today* [1] by Li pointed out that aqueous mistletoe extracts have been used as a complementary cancer drug for almost a century. With recent advances in biochemistry and molecular biology, new approaches have been used to study their anti-cancer effects. The main biological activity of the extracts has now been attributed to the mistletoe lectins (MLs). So far, one ML gene has been cloned from the European mistletoe (*Viscum album*) [2]. However, three ML chains with slightly different carbohydrate recognizing specificities and molecular weights have been isolated [3]. In addition to the European MLs, a Korean counterpart has been isolated from the subspecies (*V. album coloratum*) [4].

All of these MLs consist of a toxophoric A-chain and a carbohydrate recognizing B-chain. The A-chain is an RNA-glycosidase, which cleaves the rRNA at a specific site effectively inhibiting protein biosynthesis. Binding and internalization of MLs into cells are mediated by the B-chain, thus they are classified as type II ribosomal inactivating proteins (RIPs) [5].

Lyu [6] recently showed that the Korean ML also acts as an inhibitor of telomerase, whereas the Bax protein, an enhancer of apoptosis, is upregulated in ML-treated cells. Beyond its relevance for cancer research, this finding is also of interest for basic cell biology. It indicates that, despite the inhibition of protein synthesis by the RNA glycosidase activity of ML, there must be a mechanism, that enables protein biosynthesis for the proapoptotic proteins to continue. How this effect is achieved remains unclear, as does the question of how the bulky ML protein is transferred from the endocytotic vesicle across the lipid bilayer once it has been internalized. This transfer is a prerequisite for the action of ML on the ribosome, which is either in the cytoplasm or attached to the membrane of the rough endoplasmic reticulum.

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Polymers for drug delivery: more research needed ▼

The use of polymers in drug delivery continues to increase as clinical results show therapeutic benefits, novel applications are discovered and sources of polymers and their derivatives become more accessible. Polymers such as polyethyleneglycol and poly(styrene-co-maleic acid) now enjoy an integral role in drug delivery formulations available on the market. Yet it remains true that the biological effects of even 'biocompatible' polymers are largely unknown, perhaps because such effects seem pale in comparison to those of the drug that the polymer is helping to deliver, especially in cases where the polymer serves to mask unwanted biological responses to the drug.

It is nevertheless important to state that the biological effects of polymers should not be discounted when considering either the efficacy or safety of the whole formulation. One issue that has been particularly neglected is the effect of systemically applying polymers that are not truly biodegradable, but are too large to be cleared by renal filtration, and which will almost certainly be retained in the body long after the drug has gone.

Chemists now have the tools that make possible screening of a range of