phase known to permit ready access to enzymes. Following completion of the synthesis, incubation with a lipase allowed enzyme-induced fragmentation that released the library compounds. The quinone methide intermediate (**6**) was conveniently left attached to the resin beads where it could be trapped by water or another nucleophile.

This method has been used for the cleavage under very mild conditions of tetrahydro-β-carbolines, prepared via the Pictet-Spengler reaction, and protected thymidine derivatives.

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Emerging therapeutic targets

Molecular targets for weight control

Smoking cessation is well known to be associated with weight gain, which may be relieved by nicotine patches or gum during the withdrawal period. Activation of nicotinic acetylcholine receptors (nAChR) may modulate several neurotransmitter signalling pathways implicated in the control of body weight, including leptin, neuropeptide Y and biogenic amines. For example, a recent study demonstrated that serum leptin concentrations in smokers were significantly lower than in non-smokers – an association which was independent of diabetes status [Hodge, A.M. *et al. Int. J. Obes. Relat. Metab. Disord.* (1997) 21, 50–53]. This suggests that nicotinic signalling may modify the sensitivity of hypothalamic leptin receptors and consequently modulate leptin synthesis, thereby reducing body weight.

Selective neuropeptide Y antagonists and β_3-adrenergic agonists are being developed as weight control drugs [reviewed recently by Strader, C.D. *et al. Drug Discovery Today* (1998) 3, 250–256]. Chronic nicotine administration has been shown to reduce neuropeptide Y protein levels in the rat hypothalamus [Frankish, H.M. *et al. Brain Res.* (1995) 694, 139–146] and to increase norepinephrine turnover, a measure for sympathetic activity, in brown adipose tissue of obese mice [Yoshida, T. *et al. J. Nutr. Sci. Vitaminol.* (1990) 36, 123–130]. All these nicotinic effects have been correlated with weight loss, without affecting food intake. The nicotine-stimulated sympathetic activity on adipose tissue is also illustrated by its capacity to elevate plasma free fatty acids levels [Batt, R.A. and Topping D.L. (1979) *Int. J. Obes.* 3, 7–13].

It thus appears that with respect to weight control, nicotine might deliver the same effects as both neuropeptide Y antagonists and β_3-adrenergic agonists. However, nicotine possesses certain undesired side effects, such as induction of T cell anergy [Sopori, M.L. and Kozak, W. *J. Neuroimmunol.* (1998) 83, 148–156]. More studies are therefore required to elucidate which specific nAChR subtype(s) are involved in nicotinic body weight control, so that subtype-selective nicotinic agonists might be developed for fighting obesity, possibly alongside neuropeptide Y antagonists and β_3-adrenergic agonists.

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Bioinformatics

Learning bioinformatics

Bioinformatics is a science that essentially uses a combination of computer technology, information science and biological knowledge to collect, store, retrieve, analyse, relate and model biological data. Virtually any fact, concept or principle concerned with the biomedical sciences (this includes health, medical and biological sciences) can be included as 'biological data'. Of course, DNA, RNA and protein sequence data has considerably increased this pool of data. It is this sequence data, and its subsequent analysis by bioinformatics, that attracts most attention because it promises a considerable reduction in both time and cost for drug discovery. Consequently, trained research and scientific staff are needed to extract meaning from this complex and growing mountain of biomedical and sequence data.

Aims of training

The aims of training in bioinformatics are to enable the scientist to understand what bioinformatics can achieve and to use (or develop) bioinformatics tools effectively. These aims enhance communication and promote effective problem solving skills. Communication is particularly important between a computer scientist (who designs the computer applications) and a biological scientist (who needs to extract biologically relevant information). Consequently, much of industry bioinformatics training is really cross training of existing professionals – training computer scientists in biology and biologists in computer science.

Courses available

Mainstream bioinformatics courses are offered mainly for undergraduates and postgraduates at university. Most undergraduate courses in disciplines such as chemistry, molecular biology, biochemistry and computer science now offer units in bioinformatics, but very few (as yet) offer a full degree. Some academic and industry practitioners think it's 'too early' for institutions to develop a full degree course in bioinformatics, because the science is advancing so rapidly that it would be difficult for a degree course to keep up to date.

Presently, it seems that the preferred option for training is through either a professional (non-degree) course, a graduate course (i.e. as a 'unit' contributing to a higher degree), or a postgraduate degree such as an MSc or PhD in bioinformatics. Staff can be trained by

