PublisherInfo		
PublisherName	:	BioMed Central
PublisherLocation	:	London
PublisherImprintName	:	BioMed Central

Putting the sea into cancer therapy

ArticleInfo		
ArticleID	:	4164
ArticleDOI	:	10.1186/gb-spotlight-20010806-01
ArticleCitationID	:	spotlight-20010806-01
ArticleSequenceNumber	:	235
ArticleCategory	:	Research news
ArticleFirstPage	:	1
ArticleLastPage	:	2
ArticleHistory	:	RegistrationDate : 2001–08–06 OnlineDate : 2001–08–06
ArticleCopyright	:	BioMed Central Ltd2001
ArticleGrants	:	
ArticleContext	:	130592211

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Under normal circumstances DNA mutations occurring in a cell are fixed by the cell's own DNA-repair mechanisms. These include nucleotide-excision repair (NER), which removes damaged sections of DNA and replaces them with the correct sequence. In the August Nature Medicine, Yuji Takebayashi and colleagues from the US National Cancer Institute, Bethesda, Maryland demonstrate a new cell-killing mechanism mediated by NER that can be exploited to improve cancer therapy (*Nature Med* 2001, **7:**961-966).

Takebayashi *et al.* studied the effects of the novel anticancer drug ecteinascidin 743 (Et743), a natural product isolated from the Caribbean sea squirt (*Ecteinascidia turbinate*), on cells with the chromosome alterations seen in Xeroderma pigmentosum - a hereditary condition in which the affected individual is chronically hypersensitive to UV light. They found that Et743 alters the NER process, and rather than repairing the damaged DNA it causes the NER machinery to create lethal breaks in the DNA, thus killing cells.

This is a unique and previously unrecognised mechanism of killing cancer cells and the authors suggest that Et743 could be of considerable use in the treatment of cisplatin-resistant ovarian carcinoma, a cancer which exhibits enhanced NER activity.

References

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