

## Poison pen letters

By Lev Osherovich, Senior Writer

Researchers at **The University of Queensland** were using RNAi to knock down tumor-specific proteins when they encountered an unexpected finding: the RNAi itself stimulated immunity against tumor antigens. The work suggests RNAi could be used to flag cancer cells for detection by the immune system, potentially creating a new strategy for therapeutic cancer vaccination.<sup>1</sup>

Marine tumor cells that had been transformed with human papillomavirus (HPV), which causes cervical cancer, were treated with small hairpin RNAs designed to inactivate viral transcripts. The researchers found that the viral transcripts targeted by shRNAs were not totally destroyed, as would be expected based on previous shRNA studies. Instead, small fragments of these transcripts underwent translation, producing tiny fragments of HPV proteins. These fragments, in turn, were presented as surface antigens by the tumor cells.

"There's a hidden mechanism by which shRNA leaves messages cleaved but not destroyed," said Nigel McMillan, associate professor of cancer, immunology and metabolic medicine at the University of Queensland. "We've found that some of these messages turn out to be translated, generating epitopes that are expressed in cancer cells only."

McMillan's team went on to show that tumor cells bearing these surface epitopes elicited an immune response that protected mice. Mice injected with tumor cells treated *ex vivo* with anti-HPV shRNAs had smaller tumors than mice given untreated control tumor cells. Untreated tumor cells that were subsequently injected into the mice failed to take hold, presumably due to the animals' acquired immune response against tumor antigens.

Results were published in *Proceedings of the National Academy of Sciences*.

Altogether, the findings suggest that shRNA leads to the production of immunogenic protein fragments that alert the immune system to the presence of tumor cells.

McMillan believes that the adaptive immune system is critical for the process. "When we repeated these experiments with immunocompromised mice, it didn't work," he told SciBX.

The study presents a new use of RNAi to elicit an indirect protective effect rather than to simply kill tumor cells, said Ian MacLachlan, CEO of RNAi delivery company **Tekmira Pharmaceuticals Corp.**

"Typically when one uses an RNAi-mediated means of affecting tumor growth or progression, you're knocking down a tumor-related target to slow growth," said MacLachlan. "Here, they're trying to elicit an immune response against the tumor."

### Raise the alarm

The RNAi approach for priming an immune response to tumors may have one major advantage over protein-based cancer vaccines: the ability to target a wide range of cancer antigens in a single formulation. The breadth of coverage is important for overcoming antigenic escape by rapidly mutating tumors.

"Cancers will mutate away target sites as fast as they can, so we should have three or four targets," said McMillan.

Although cancer vaccines with multiple proteins have been attempted, selecting and formulating the right tumor antigens is technically challenging and varies between indications. In contrast, the specific targets of an RNAi vaccine could be customized for each patient based on the tumor's gene expression profile.

An RNAi vaccine could also be more useful for personalized tumor therapy than protein vaccines because making customized RNAi cocktails based on an individual patient's tumor protein expression patterns is, in principle, easier than formulating complex mixtures of recombinant proteins.

However, the RNAi approach faces many of the same hurdles as protein-based vaccines, such as how and when to deliver the vaccine and how to measure efficacy.

Two companies have recently reported promising results with their respective cancer vaccines. **Dendreon Corp.**'s Provenge sipuleucel-T met its survival endpoint in a Phase III prostate cancer trial.<sup>2</sup> Last month, **Antigenics Inc.** reported data from an extension of a Phase III trial that showed increased survival in kidney cancer patients receiving the company's Oncophage vitespen.

Oncophage uses heat shock protein GP96 and associated peptides isolated from the patient's tumor. Provenge is composed of autologous dendritic cells loaded with a fusion protein of prostatic acid phosphatase and an immunostimulatory cytokine.

Andrew Parsa, associate professor of neurological surgery at the **University of California, San Francisco**, described the RNAi vaccination method as less direct than vaccinating with tumor-associated proteins such as GP96.

"This is the long road to doing what the heat shock protein vaccine does," said Parsa.

Parsa is primary investigator on a Phase II trial of Oncophage for primary glioblastoma, which the company said is enrolling patients. A Phase I trial of Oncophage in recurrent, high-grade glioma showed an increase in mean survival time, according to Antigenics.

Parsa noted that Oncophage is aided by the presence of specific receptors for tumor-derived GP96 on immune cells. In contrast, an RNAi-based approach still would require tumor-derived protein fragments to be taken up by professional antigen-presenting cells such as dendritic cells.

"Heat shock proteins are a natural part of our immune response. They have a lock and key mechanism for getting antigens to the presenting cells," said Parsa. "Almost every other approach requires there to be an almost random mechanism for delivering the vaccine to the correct immune cells."

# Poison Pen Letters

**Great Britain. Law Commission**



## **Poison Pen Letters:**

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way I really hope there is more to come from the Village Detectives An entertaining read Reader Review A brilliant beginning to a new series Reading a book written by Fiona Walker is like visiting an old friend Lots of good memories and wanting to make more Can t wait for the next Village Detectives book Delightful enjoyable read Reader Review [Report on poison-pen letters](#) Great Britain. Law Commission,1985 **Poison Pen Letters to Myself** Romany Rivers,2014-05-30 Poison Pen Letters to Myself chronicles a very personal journey through the years overcoming severe bouts of depression and consequently creating a more holistic and spiritual lifestyle The chapters Red Letters Return to Sender and Addressee Unknown reveal periods of depression and anxiety anger and healing and acceptance and spiritual growth The words in these pages were not written for mass consumption They were not artfully crafted for reading aloud in dim rooms to a soundtrack of clicking fingers and Parisian style applause They were not intended as political statements or a way of reaching other wayward wandering souls Over the last two decades they were poured purged scribbled and spat onto scraps of paper napkins backs of hands into empty pages and blank spaces of other books At times of sorrow frustration confusion acceptance and joy these words made sense of the minds muddled meanderings Within these pages you will find heart breaking heart healing honesty that crosses the divide and touches the souls of others *Criminal Law* Great Britain. Law Commission,1985 *Poison Pen Letters* Toby Tripp,2003-01-01 **Penning Poison** Emily Cockayne,2023 This book is about anonymity emotion and detection Gathering surviving anonymous letters penned in England between 1760 1939 together it identifies possible authors and explores the impact they had on individuals and communities charting how developments in postal services detection and the media influenced writers and their targets **Penelope Barrows #3 the Case of the Poison Pen Letter** C. C. Beechum,2012-07-24 The only thing I was worried about was my mail My fear was caused by a letter that I received on a very hot day in August upon arriving home from Chicago It was addressed to me Miss Penelope Barrows but when I opened the envelope the paper inside was blank Blank Now I don t know why someone would send me a letter with a blank piece of paper in it but I was sure willing to find out I mean a letter with nothing written on it is not a common thing Why would someone do this What could be the reason **The Mystery of the Poison Pen Letters** S. K. Velu,1992 [Points of Entry](#) Vic Satzewich,2015-09-01 Every year over 1 3 million people apply to visit work or settle in Canada It falls to visa officers to determine who gets in and who stays out In the face of this enormous responsibility how do these gatekeepers use their discretionary authority to assess eligibility credibility and risk Seeking answers to this question Vic Satzewich conducted interviews with 128 visa officers locally engaged staff and immigration program managers at eleven overseas offices He reveals how the organizational context within which they work shapes their decision making When something in an application does not add up somber photographs from a supposed wedding celebration for example an officer conducts follow up interviews with the applicant In a world where no two visa applications are the same and in the context of complex and shifting population movements and pressures this is a fascinating look at how visa officers do their

work The American Penman, 1922 **Kind Regards** Liz Williams, 2012-09-06 Despite the ever growing influence of technology handwritten letters are regaining their value meaning and popularity *The Propaganda Warriors* Clayton David Laurie, 1996 A fascinating story Essential to an understanding of America's use of propaganda Warren F Kimball author of *The Juggler Franklin Roosevelt as Wartime Statesman* Lively and revealing There is much that is new and important in this book All students of the war as well as of intelligence will benefit from it Robin W Winks author of *Cloak and Gown* A must acquisition for anyone with any interest in espionage intelligence and propaganda Dennis Showalter author of *Tannenburg Clash of Empires* *British Genres* Marcia Landy, 2014-07-14 In this unprecedented survey of British cinema from the 1930s to the New Wave of the 1960s Marcia Landy explores how cinematic representation and social history converge Landy focuses on the genre film a product of British mass culture often dismissed by critics as unrealistic showing that in England such cinema subtly dramatized unresolved cultural conflicts and was in fact more popular than critics have claimed Her discussion covers hundreds of works including historical films films of empire war films melodrama comedy science fiction horror and social problem films and reveals their relation to changing attitudes toward class race national identity sexuality and gender Landy begins by describing the status and value of genre theory then provides a history of British film production that illuminates the politics and personalities connected with the major studios In vivid accounts of the films within each genre she analyzes styles codes and conventions to show how the films negotiate history fantasy and lived experience Throughout Landy creates a dynamic sense of genre and of how the genres shape not merely reflect cultural conflicts Originally published in 1991 The Princeton Legacy Library uses the latest print on demand technology to again make available previously out of print books from the distinguished backlist of Princeton University Press These editions preserve the original texts of these important books while presenting them in durable paperback and hardcover editions The goal of the Princeton Legacy Library is to vastly increase access to the rich scholarly heritage found in the thousands of books published by Princeton University Press since its founding in 1905 *New York Court of Appeals. Records and Briefs.* New York (State). Court of Appeals., 1951 Volume contains need index past index 6 *Tschumi v Hayward* need index past index 6 *Tschumi v Hayward* need index past index 6 *Tschumi v Hayward* need index past index 6 207 17 West 25th St Co Inc v Blu Strike Safety Razor Blade Co Inc need index past index 6 207 17 West 25th St Co Inc v Blu Strike Safety Razor Blade Co Inc need index past index 6 207 17 West 25th St Co Inc v Blu Strike Safety Razor Blade Co Inc need index past index 6 207 17 West 25th St Co Inc v Blu Strike Safety Razor Blade Co Inc need index past index 6 *Valentine v State of N Y* need index past index 6 *Valentine v State of N Y* need index past index 6 *Washington v State of N Y* need index past index 6 *Washington v State of N Y* need index past index 6 *Weintraub v Weintraub* need index past index 6 *Wekstein v Herald Statesman* need index past index 6 *Wekstein v Herald Statesman* need index past index 6 *Wekstein v Herald Statesman* need

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## Reviewing **Poison Pen Letters**: Unlocking the Spellbinding Force of Linguistics

In a fast-paced world fueled by information and interconnectivity, the spellbinding force of linguistics has acquired newfound prominence. Its capacity to evoke emotions, stimulate contemplation, and stimulate metamorphosis is really astonishing. Within the pages of "**Poison Pen Letters**," an enthralling opus penned by a very acclaimed wordsmith, readers attempt an immersive expedition to unravel the intricate significance of language and its indelible imprint on our lives. Throughout this assessment, we shall delve to the book is central motifs, appraise its distinctive narrative style, and gauge its overarching influence on the minds of its readers.

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verschwunden vanished without a trace spurlos verschwunden

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