

unaware of any reports that patients treated with these drugs have become susceptible to novel suppression-mediated transpositions.

Second, the frequency with which transposons are inactivated solely by a single nonsense mutation is quite low.⁴ PTC124 does not suppress mRNAs containing more than one premature nonsense codon.¹

Third, almost all transposons harbouring a nonsense mutation have also accumulated additional mutations,⁴ presumably owing to a lack of selective pressure on these retroelements to maintain protein-coding potential. PTC124 does not correct protein production in transcripts containing conventional insertional, deletional, or mis-sense mutations⁵—ie, PTC124 is incapable of promoting the production of full-length proteins from such elements.

Finally, as Goodier and Mayer state, nonsense mutations are not always deleterious. Such mutations can mute genetic noise by promoting the degradation of nonsense-containing transcripts through the process of nonsense-mediated mRNA decay.⁵ Because PTC124 promotes nonsense suppression, but does not affect the nonsense-mediated mRNA decay pathway,¹ levels of nonsense-containing transcripts are not affected by this compound.

In short, there is little scientific evidence to support the concept of retroelement activation by a drug such as PTC124.

EK and BK received funding support from PTC Therapeutics for this study. EMW, CT, MW, LM, and SWP are employees of PTC Therapeutics. AJ has no conflicts of interest.

*Eitan Kerem, Batsheva Kerem, Ellen M Welch, Christopher Trotta, Marla Weetall, Langdon Miller, Allan Jacobson, Stuart W Peltz
kerem@hadassah.org.il

Hadassah Hebrew University Hospital, Jerusalem, Israel (EK); Department of Genetics, Life Sciences Institute, Hebrew University, Jerusalem, Israel (BK); PTC Therapeutics, South Plainfield, NJ, USA (EMW, CT, MW, LM, SWP); and Department of Molecular Genetics & Microbiology, University of Massachusetts Medical School, Worcester, MA, USA (AJ)

- 1 Welch EM, Barton ER, Zhuo J, et al. PTC124 targets genetic disorders caused by nonsense mutations. *Nature* 2007; **447**: 87–91.
- 2 Hirawat S, Welch EM, Elfring GL, et al. Safety, tolerability, and pharmacokinetics of PTC124, a non-aminoglycoside, nonsense mutation suppressor, following single- and multiple-dose administration to healthy male and female adult volunteers. *J Clin Pharmacol* 2007; **47**: 430–14.
- 3 Howard M, Frizzell RA, Bedwell DM. Aminoglycoside antibiotics restore CFTR function by overcoming premature stop mutations. *Nat Med* 1996; **2**: 467–69.
- 4 Seleme MC, Vetter MR, Cordaux R, Bastone L, Batzer MA, Kazazian HH. Extensive individual variation in L1 retrotransposition capability contributes to human genetic diversity. *Proc Natl Acad Sci USA* 2006; **103**: 6611–16.
- 5 Mendell JT, Sharifi NA, Meyers JL, Martinez-Murillo F, Dietz HC. Nonsense surveillance regulates expression of diverse classes of mammalian transcripts and mutes genomic noise. *Nat Genet* 2004; **36**: 1073–78.

Humanitarian crisis in Vanni, Sri Lanka

Oliver Johnson and co-authors (March 7, p 809)¹ correctly point out that there is a humanitarian crisis in Sri Lanka and we are thankful to them for bringing up this important issue.

However, their letter contains some inaccuracies. The UN's announcement that cluster bombs were used on Puthukkudiyiruppu Hospital created major international concern, but the remark was later withdrawn² and the UN resident coordinator extended an apology.

Johnson and colleagues also report that humanitarian organisations have been banned by the Sri Lankan Government. The reference given for this statement actually states that “the government told all NGOs and UN to leave the area”.³ All these organisations are now based in Vavuniya, just outside the area of intense war. Not a single non-governmental organisation has actually been “banned”.

Johnson and colleagues further express their concern over people entering government-held territory and being forced to remain in detention camps. However, they do not mention that terrorists are keeping civilians as hostages and have launched several attacks⁴ on those who try to escape from the war zones. The UN humanitarian chief, after a 3-day visit

to this area, urged the Liberation Tigers of Tamil Eelam to allow civilians to leave the conflict area.⁵

We Sri Lankans are indeed in a crisis. In order not to make it worse, we urge the international medical community to analyse carefully the facts presented about our stricken country and help Sri Lanka to overcome this major problem.

I declare that I have no conflicts of interest.

Suneth Agampodi
sunethagampodi@yahoo.com

Department of Community Medicine, Faculty of Medicine and Allied Sciences, Rajarata University of Sri Lanka, Anuradhapura, Sri Lanka

- 1 Johnson O, Ratneswaren A, Beynon F. Humanitarian crisis in Vanni, Sri Lanka. *Lancet* 2009; **373**: 809–10.
- 2 Amnesty International. Update on reported use of cluster munitions in attack on hospital. <http://www.amnesty.org/en/for-media/press-releases/sri-lanka-cluster-bomb-strike-hospital-despicable-20090204> (accessed April 6, 2009).
- 3 Médecins Sans Frontières. Sri Lanka: 250,000 civilians trapped in intense fighting. http://www.msf.org.uk/civilians_trapped_in_sri_lanka_20090128.news (accessed March 9, 2009).
- 4 UN. UN relief chief concerned over physical condition of Sri Lankans trapped by clashes. <http://www.un.org/apps/news/story.asp?NewsID=30046&Cr=sri+lanka&Cr1=> (accessed March 9, 2009).
- 5 UN. On visit to Sri Lanka, UN humanitarian chief stresses need to protect civilians. <http://www.un.org/apps/news/story.asp?NewsID=29954&Cr=sri+lanka&Cr1> (accessed March 9, 2009).

Assessment of childhood immunisation coverage

Stephen Lim and colleagues (Dec 13, p 2031)¹ recommend that, in the era of performance-based financial initiatives such as GAVI Alliance's immunisation services support (ISS), health indicators should be monitored by independent surveys rather than administrative data-monitoring systems.

However, Lim and colleagues' estimates for immunisation coverage during the period after the onset of ISS in some low-income countries such as Cameroon are heavily weighted by pre-ISS survey data. Such estimates assume that ISS did not have an effect on the performance of immunisation programmes—an assumption that is not supported by a closer look at immunisation data from Cameroon.

The printed journal includes an image merely for illustration

PA Photos

See [Editorial](#) page 1399
See [Department of Error](#) page 1428