More Powerful Hurricanes to Come

By Cynthia Chi

Hurricanes Katrina and Rita made headlines this year as they tore through the Gulf Coast. However, they may represent only the beginning of a trend of increasingly powerful hurricanes. In the past, researchers have linked global warming and the rise of sea surface temperatures (SST) to an increase in the number and intensity of tropical cyclones in the Atlantic and Pacific Oceans. However, this link is not definitive and requires more studies of the effects of SST on hurricane formation (1).

▲ A satellite image of Hurricane Isabel, a Category 5 hurricane that resulted in 17 deaths and over 3 billion dollars of damage to the United States Atlantic coastline in 2003.

Since 1970, scientists have been using satellites to analyze trends in hurricane number and intensity. In the past 35 years, the changes in the frequency and duration of tropical cyclones in all ocean basins have been statistically insignificant except in the North Atlantic, where an increase in both the frequency and duration of hurricanes has been observed (2).

More importantly, a clear trend toward more intense storms has been observed in all ocean basins. Storm intensity is measured using several different methods, including the Saffir-Simpson scale and the calculated power dissipation index (PDI), which is based on total power dissipation integrated over a cyclone's lifetime and which is calculated from wind speeds. Over the past 35 years, the number of category one, two, and three tropical storms on the Saffir-Simpson scale has remained the same but has decreased as a percentage of the yearly number of tropical cyclones. In contrast, although the maximum wind speed each year has remained constant, the strongest storms – those of categories four and five – have almost doubled both in number and as a percentage of the yearly number of storms (2). Furthermore, the PDI of storms in the North Atlantic and North Pacific has increased more than two-fold since the 1970s (3).

Many researchers have begun to link the trend in increasing hurricane intensity to a rise in sea surface temperature (SST). Generally, increases in SST have been attributed to global warming, and the average SST has seen a 0.5°C increase in all ocean basins (2,3,4). Increasing SST, more frequent North Atlantic hurricanes, and a higher proportion of intense storms all appear to be correlated with global warming. According to Webster *et al.*, SST is likely not related to storm frequency; however, the correlation between SST and storm intensity cannot be ruled out (4). Similarly, Kerry Emanuel argues that year-to-year PDI and SST have shown a strong correlation over the past 50 years. However, there are many factors other than global warming that affect storm intensity, such as the temperature profile of the troposphere, the lowest region of the Earth's atmosphere, and vertical wind shear (3).

Kevin Trenberth relates global warming to storm intensity by way of increasing water vapor in the lower troposphere. He argues that global warming and higher SST increase water vapor, which in turn increases the energy in the lower troposphere that is available to developing hurricanes (4). Although he does not draw a definite correlation between increasing water vapor and the number of storms, he claims that high water vapor provides more energy to fuel storms that have already formed, a notion that is consistent with the unchanging frequency and increasing intensity of hurricanes (5).

Problems in these analyses arise from insufficient data on tropical cyclones worldwide. Satellites use pattern recognition programs to estimate cyclone intensities throughout the world, but the only areas with aircraft reconnaissance to accurately measure wind speeds are the North Atlantic, which accounts for only 12% of the world's storms, and more recently, the North Pacific (1,2). Hurricanes in the Atlantic could respond very differently to environmental changes than hurricanes in other parts of the

credit: National Oceanic and Atmospheric Administration

world, making any conclusions and correlations uncertain. Current research is investigating how oceans interact with atmospheric changes worldwide in order to determine the causes of storm patterns in the various ocean basins (1).

—Cynthia Chi '08 is a Chemistry and Physics concentrator in Winthrop House.

1. Schiermeier, Quirin. "Hurricane link to climate change is hazy." *Nature* 437 (22 Sep 2005): 461.
2. Webster, P. J., *et al*. "Changes in tropical cyclone number, duration and intensity in a warming environment." *Science* 309 (16 Sep 2005): 1844-1846.
3. Emanuel, Kerry. "Increasing destructiveness of tropical cyclones over the past 30 years." *Nature* 436 (4 Aug 2005): 686-688.
4. Trenberth, Kevin. "Uncertainty in hurricanes and global warming." *Science* 308 (17 Jun 2005): 1753-1754.
5. Schiermeier, Quirin. "Trouble brews over contested trend in hurricanes." *Nature* 435 (23 Jun 2005): 1008-1009.

Nipping the Virus in the Bud

Developments in antiviral RNAi therapy

By Shirleen Soh

Despite being a relatively new technology, RNA interference (RNAi) has rapidly developed into a promising approach to curing disease by reducing the expression of disease-causing genes. To date, RNAi has been found to successfully inhibit the expression and replication of a broad range of human and mammalian viruses *in vitro*, including the human immunodeficiency virus (HIV), Marburg virus, poliovirus, and severe acute respiratory syndrome (SARS) virus (1). The first successful use of RNAi therapy against a viral infection in a living organism occurred in 2003, when Song *et al.* showed that RNAi can alleviate hepatitis in mice (2). This year, Bitko *et al.* described a novel method of RNAi delivery that successfully inhibited respiratory viruses in mice (3).

Traditionally, viral infections have been treated using protein-based drug therapies, whereby a drug inhibits the activity of a protein that is made by, or associated with, the virus. Viruses rely extensively on host proteins for replication and transmission; thus, targeting these proteins often results in unwanted side effects on normal cell processes. RNAi is especially well suited to antiviral therapy, as it depends on the recognition of a short sequence of viral target RNA. It is therefore able to discriminate easily between virus and host, avoiding the problems associated with targeting viral proteins that might resemble host proteins. Furthermore, RNAi provides what is potentially the most rapid method of combating a new disease, as the development of RNAi therapeutics can begin once the genome of the virus has been sequenced. This was most recently demonstrated by the investigations into RNAi therapy against the SARS virus in 2004 (4). By acting against mRNA before it is translated into protein, RNAi therapy eliminates the need to wait until the activity of the relevant protein has been elucidated before protein-based therapies can be developed.

RNAi therapy typically involves the introduction of small interfering RNAs (siRNAs) that bind to short sequences in the viral genome into the cell that is infected or about to be infected. Several *in vivo* studies on cell lines have reflected tremendous potential for this method. For instance, Fowler *et al.* have shown that siRNA inhibition of the Marburg virus lowered viral protein production to almost undetectable levels, as compared to controls (5).

Despite its promise, RNAi therapy faces several challenges before it can be used on a large scale. One challenge is the ability of viral genomes to mutate rapidly, allowing them to evade binding by siRNAs. Song *et al.*, who demonstrated the first successful use of RNAi therapy *in vivo*, circumvented this problem by targeting mRNA transcripts of cellular recruits of viral infection, rather than the viral proteins themselves (2). Specifically, they targeted the Fas cell surface receptor, which mediates cell death in case of injury to the liver. Injection of the siRNA into the bloodstream resulted not only in decreased production of the target protein, but, most significantly, in the prevention of any clini-

cal signs of infection when RNAi was administered before infection, and in a marked decrease in clinical indicators of infection when RNAi was administered after chronic infection.

Another challenge for RNAi therapy, as with all other therapies, is delivery. All drugs must be able to reach and enter affected cells intact if they are to have any effect. Song *et al.* showed that injection into the bloodstream is an effective means of siRNA delivery (2). An even more interesting method is that used by Bitko *et al.*, who delivered siRNAs by aerosol inhalation (3). This method of delivery was shown to successfully prevent and treat respiratory infections, suggesting that intranasal application of siRNA is a potentially viable approach to curing pulmonary viral infections in humans. Moreover, 70-80% effectiveness was demonstrated for pure, naked siRNA relative to siRNA delivered with a transfection agent, or a compound that facilitates entry of siRNA into cells (3). Therefore, in addition to being painless and non-invasive, intranasal delivery has the advantage of not requiring a transfection agent, which in some cases has been shown to cause side effects. This study is one of many that show the promise of RNAi as an effective antiviral therapy. H

—Shirleen Soh '08 is a Biology concentrator in Winthrop House.

1. Leonard, J.N. and Schaffer, D.J. "Antiviral RNAi therapy: emerging approaches for hitting a moving target." *Gene Therapy* (2005): 1-9.
2. Song, E. *et al*. "RNA interference targeting Fas protects mice from fulminant hepatitis." *Nature Medicine* 9.3 (2003): 347-351.
3. Bitko, V. *et al*. "Inhibition of respiratory viruses by nasally administered siRNA." *Nature Medicine* 11.1 (2005): 50-55.
4. Wu, C. *et al*. "Inhibition of SARS-CoV replication by siRNA." *Antiviral Research* 65 (2005): 45-48.
5. Fowler, T. *et al*. "Inhibition of Marburg virus protein expression and viral release by RNA interference." Journal of *General Virology* 86 (2005): 1181-1188.