New agent strikes at respiratory syncytial virus replication

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University of Texas Medical Branch at Galveston researchers have achieved promising results with a potential new weapon against respiratory syncytial virus, the most common cause of infant hospitalization in the United States.

In an effort to find an effective antiviral therapy for RSV, the scientists tested two types of complex, custom-designed molecule to interfere with the genetic machinery that RSV uses to replicate, or copy itself, within cells. Both of the so-called “morpholino oligomers,” created by Oregon-based AVI BioPharma, penetrated cultured human airway cells easily and produced only minimal toxicity. One of the two, designated AUG-2, significantly reduced RSV replication in both cell culture and mouse experiments.

“Viral replication is one of the major pathogenetic processes of RSV, and we badly need a specific antiviral therapy,” said UTMB Dr. Roberto Garofalo, senior author of a paper on the study to be published in the June issue of *Molecular Therapy* and now available in the “Advance Online Publication” section of the journal’s website. “That's what an agent like this morpholino could give us.”

RSV infects almost all children by age two, but normally causes only a cold-like upper respiratory infection. In some babies, however, it spreads to the lungs, where the inflammation it generates causes coughing, wheezing and extreme difficulty in breathing, a life-threatening clinical syndrome known as bronchiolitis.

Recent research by Garofalo and other investigators suggests that two key factors drive RSV bronchiolitis: an inflammatory overreaction by the cells that line the airways of the lungs, and a failure to respond to RSV by T lymphocytes (also known as “T cells”), immune system cells that ordinarily act to control viral infections.

Because a dangerous inflammatory response occurs so soon after RSV begins replicating in the lungs, Garofalo said, antiviral therapy by itself is unlikely to be sufficient to treat severe RSV infection in infants. But it could be a critical part of a “combination therapy” that also included drugs to reduce RSV-induced lung inflammation and boost T-cell response.

“The virus continues to replicate for days in the lungs of infected infants, and it induces inflammation as long as it replicates,” Garofalo said. “So stopping viral replication would be a very important part of any therapeutic strategy for RSV.”

Source: University of Texas