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### Small molecule activation of APOBEC3G host defense

APOBEC3G (A3G) is a protein expressed in human cells that serves as an antiviral host-defense factor. While the majority of studies have suggested that A3G DNA mutagenic activity on nascent single stranded proviral DNA inhibits viral replication, recent studies suggested that circumstances might exist in permissive cells where A3G mutagenic activity may benefit the virus and promote the emergence of drug-resistant strains. We have identified small molecules for therapeutic development that are also novel research tools for addressing the urgent question of whether endogenously expressed A3G deaminase activity can be modulated to exceed a mutagenic threshold necessary for it to have antiviral activity. This is a relevant question because, in permissive cells, A3G is almost entirely 'switched off' through its interaction with cellular RNA and this low level of activity may benefit the virus. Compounds have been identified that activate A3G deaminase activity by dissociating RNA from the enzyme and these compounds had a dose-dependent antiviral effect in permissive cells where A3G was sequestered as high molecular mass complexes. These compounds are first in their class and show that RNA inhibition of A3G is reversible in living cells. These compounds also hold the potential to preemptively inhibit HIV post-entry by making cellular A3G more effective as antiviral without the need for A3G to become encapsidated. As such A3G activators may have utility in disease prevention.

#### Biography

Harold C. Smith is a graduate of Purdue University and holds graduate degrees from Purdue and the State University of NY at Buffalo. He carried out postdoctoral studies at Baylor College of Medicine, Houston, TX. He is professor of Biochemistry and Biophysics with the University of Rochester. He has published more than 100 papers in reputed journals and contributes to curriculum development and teaching of undergraduates, graduate students and medical students at the University. He is also founder and Chief Scientific Office of OyaGen, Inc.