Michele Pagano Selected as Howard Hughes Medical Institute Investigator

**New York, NY - May 27, 2008:** The Howard Hughes Medical Institute announced today that Dr. Michele Pagano, the May Ellen and Gerald Ritter Professor of Oncology in the NYU Department of Pathology, is among the 56 top scientists who will be appointed as HHMI Investigators this year. The selection ranks as one of the highest honors that can be bestowed on a biomedical research scientist, because HHMI offers its investigators the resources and the freedom to explore their own lines of inquiry. Appointees are selected for their creativity, their innovative ideas, and their productivity. They are granted the flexibility to follow their scientific instincts and take risks rather than relying on specific research grants for predefined projects. In doing so, the philanthropy aims to encourage scientists to “extend the boundaries of knowledge” and to “pursue challenging questions” that make fundamental scientific discoveries possible.

HHMI Investigators are chosen through rigorous and intense competitions in a highly selective review process. There are currently about 300 scientists who lead Hughes laboratories at 64 institutions. Founded in 1953 by Howard R. Hughes, the aviator and industrialist, HHMI is one of the largest philanthropies dedicated to the betterment of human health. For the research support of its Investigators, the Institute is committing more than $600 million over their first term of appointment.

Michele Pagano was among those selected from more than one thousand applications. His research explores the roles that the ubiquitin system plays in cell proliferation, differentiation, and death, and how the deregulation of the system can cause cancers.

Since he joined the NYU Department of Pathology, Pagano has been working on the ubiquitin system, which is part of the cell’s recycling organization. F-box proteins are subunits of the SCF ubiquitin ligase family of enzymes and are almost ubiquitous in the cell’s workings, seemingly everywhere and doing everything. Ubiquitin is attached as a “tag” to proteins that have completed their cellular tasks or are worn out, misfolded, or in surplus. Once
proteins are tagged by ubiquitin, they are degraded back into amino acids by cellular grinders called proteasomes. F-box proteins make sure that these ubiquitin tags are stuck onto the right “molecular waste.” Thus, their job takes F-box proteins everywhere and brings them on the scene during the cell’s most delicate operations. That’s what would be expected from the cell’s waste management system.

Yet, not everyone expected this family of orphan proteins to wield power over so many important cellular processes. Pagano's research group has revealed that F-box proteins help control cell proliferation, DNA-damage checkpoints, chromosomal stability, ribosomal biogenesis, protein synthesis, apoptosis, neurogenesis, and even the setting of the circadian clock.

Pagano has also found that many F-box proteins have connections to cancer. They play key roles in both tumor suppression and tumor activation. He discovered that low levels of certain F-box proteins were by themselves a warning that a tumor may be developing. In other cases, such as in breast cancer, Pagano demonstrated that high levels of one particular F-box protein represent a diagnostic sign that the cancer is of a highly aggressive form. Raising levels of a different F-box protein seems instead to sensitize tumors to certain anticancer drugs. As an HHMI investigator, Pagano intends to use his new position to refine the diagnostic signatures of F-box proteins and give more of these orphan proteins a home in the scientific world.

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