Keef wins $1.2 million grant to study the ‘unspoken affliction’

Fecal incontinence affects 15 percent of adults over 50 and costs $26 billion annually

The jokes are inevitable considering her area of research, but Kathleen Keef, professor of physiology and cell biology at the University of Nevada School of Medicine, has developed a thick skin and takes it in stride. "My immediate colleagues have been known to tease me on occasion, but I recognize it is all in good fun," she says. "The more difficult situation arises when I interact with those outside the scientific community."

Keef’s research focuses on the internal anal sphincter muscle and the causes of fecal incontinence. "The degree of social stigma and crude jokes that surround defecation and the anus is most unfortunate and is a major reason why so many who are afflicted do not seek medical help," she says, adding that studies published on this topic suggest that more than half of those afflicted do not seek medical attention.

Fecal incontinence is the inability to control one’s bowel movements, causing unexpected leaks. It may result from a
weakening of the internal or external anal sphincter muscles or from injury to the nerves that control these muscles.

Approximately five percent of the general community and 15 percent of adults over the age of 50 suffer from fecal incontinence. This disorder greatly reduces the quality of life for millions of Americans and can lead to depression, anxiety, social isolation, loss of employment and institutionalization. It can affect both children and adults but is more common in women and older adults. Obesity, decreased physical activity, diabetes and neurologic disease such as stroke are also known to increase the risk of fecal incontinence.

The combined financial burden for treating fecal and urinary incontinence in the United States exceeds $26 billion per year. However, even in 2010, fecal incontinence remains the “unspoken affliction” rarely discussed by patients and under-reported to physicians. In spite of both financial and quality of life issues, the scientific community’s understanding of the causes underlying this disorder, and the ability to prevent or treat it, remain poor.

When Keef joined the School of Medicine’s Department of Physiology and Cell Biology in 1987, her interest was in cardiovascular research. Since the focus on the internationally known department was on the gastrointestinal tract, she gradually shifted her area of research to the GI tract. She became interested in the IAS (internal anal sphincter), a specialized ring of muscle located at the end of the gastrointestinal tract that plays a central role in maintaining fecal continence.

In spite of its clear clinical relevance, the IAS is the least studied muscle in the GI tract, representing approximately 0.3 percent of the scientific literature devoted to that physiological system.

The social stigma attached to the IAS and the lack of research being done were two of the reasons Keef decided to pursue research on the muscle, in addition to her background as a cardiovascular physiologist.

“Surprisingly, I found that the IAS shares more features in common with the muscle of blood vessels than any other part of the GI tract. Thus, I have been able to apply insights from my work on blood vessels to my current work on the IAS,” she says.

Keef was recently awarded a four-year, $1.2 million grant from the National Institute of Health to study the control of motility, or contraction, in the IAS. This is her second major NIH Research Project Grant (ROI) grant in the last 10 years for research with significant implications for fecal incontinence.

Most muscles of the GI tract behave somewhat like the heart in that they contract rhythmically. This is essential for the mixing, digestion and absorption that occurs through much of the GI tract.

In contrast, the IAS muscle remains contracted most of the time, relaxing only during those brief periods of time when defecation occurs. This unique property of the IAS is associated with its anatomical and functional properties. Specifically, the muscle is organized into countless “minibundles” that each contain a set of nerves and pacemaker cells. Keef’s research has found that loss of pacemaker cells may be an important factor contributing to the development of fecal incontinence.

“By gaining a better understanding of how these unique cells maintain continence we will be in a better position to diagnose disease and devise new therapies to improve continence when it becomes compromised,” Keef says.

Her newly funded grant seeks to further explore this issue by focusing on several unique properties of the IAS including differences in the structural design of this muscle, differences in the types of cells that participate in the control of muscle contraction and differences in the mechanisms by which nerves regulate contraction of this muscle. Such information is critical for an improved understanding of the unique functional role of this muscle and for devising new strategies to help prevent, diagnose and treat problems associated with IAS dysfunction.

“Once you distance yourself from the social stigma, it turns out that the process by which this muscle manages to stay closed most of the time and open when required is unique and fascinating,” Keef said.

While at the University, Keef has obtained five major RO1 grants as well as other grants from the American Heart Association. For the past 20 years she has also served as director of the cell and tissue core of a program project grant on regulatory mechanisms in intestinal motility.

During her career, Keef has supervised 26 undergraduate students, seven medical students and has supervised the thesis projects of four graduate students. Since 1992, she has served as course coordinator of systems physiology, a course taught to first-year medical students.