Contributions of the UVA Urology Department to Product Innovation and Translational Research

A Product Born at UVA

SpermCheck Fertility is a commercially-available home sperm test. This test informs the male user if he has a normal sperm count or a low sperm count that suggests he may be infertile and should seek further evaluation. Over 40% of infertility among couples is actually due to male infertility. This test is over 98% accurate with easy-to-read results that are equivalent to laboratory testing. Currently, it is the only FDA-approved immunodiagnostic home test for sperm.

This product sits on the family planning shelves at pharmacies next to pregnancy and ovulation tests for women. It has been available at Walgreens drug stores in the USA since the summer of 2012. It is currently available at CVS-online, and beginning in June, 2014, will being carried by Rite Aid stores in the US. SpermCheck is also available at Boots, the predominate drug and pharmacy chain in Britain--and it is CE marked, or has approval as a drug product marketed in the EEA. In addition, Health Canada—the Canadian governmental department overseeing public health—has approved the product, which can be found in Walmart, Rexall and other fine pharmacies throughout the nation.

Moreover, this product contributes to the societal and economic "virtuous cycle" of public benefit in some crucial ways:

- It helps men privately realize and understand their essential contribution to infertility and to seek medical treatment if necessary. Thus, it brings a measure of gender equity to family planning.
- It helps both women and the medical profession: Women will feel less burdened to assume responsibility for infertility, and are less likely to undergo unnecessary medical tests.
- The product, from lab to manufacturing to distribution, is entirely grown and made in the USA. Accordingly, it truly symbolizes innovation, jobs, validation for NIH-funded research--and the belief in possibilities.

The Research Background at UVA

The commercial introduction of this test is the result of a basic and translational science effort. The process involved interdisciplinary research and a long history of NIH grant support in proteomics and genomics research of human spermatogenesis at UVA. The two principals involved were Dr. Stuart Howards, a UVA urologist who specializes in male infertility; and Dr. John Herr, a cell biologist and biomedical engineer at UVA, whose basic scientific research was examining the human sperm proteome. These two individuals performed collaborative, NIH-sponsored research for almost two decades.

About 20 years ago, Dr. Stuart Howards suggested to Dr. John Herr that there was a critical need for a home sperm test because men who are partners in an infertile marriage are reluctant to go to a physician to be evaluated. Meanwhile, Dr. Herr was involved in basic research looking for testis-specific genes.

Over time, this interdisciplinary partnership lead to the development of a precise, FDA-approved home sperm test.

Discovery of a Biomarker for Sperm

As a critical early chapter in this story, the researchers discovered a testis and sperm specific protein, SP-10, and its encoding gene, ACRV1.

Among all the organs in the body, the protein molecule SP-10 was revealed to be restricted only to the testis. The SP-10 protein was found only at the last steps of the developmental sequence of sperm in the testis—namely, at the transition of round spermatids into mature sperm cells. Specifically, the SP-10 protein was found only in the latter stages of spermatid growth that involve formation of the acrosome, an organelle on the surface of the sperm head.

Over a 20 year period, during which more than 31 basic and clinical papers were published, a series of discoveries were made that qualified the SP-10 protein as a valid, testis-specific biomarker for sperm. In science, a biological marker—or *biomarker*—is a measurable substance [sometimes called an analyte] in an organism whose presence is indicative of some related phenomenon such as disease, infection, or environmental exposure. *It was discovered that the concentration of the SP-10 protein in a sample of semen, if measured correctly, is proportional to the number of sperm present.*

This biomarker discovery eventually lead to the development SpermCheck Fertility, a commercial, immunodiagnostic test for detecting male infertility.

A Trail from Research to Product

As suggested, finding the right protein to serve as a biomarker was not a short process. The research team sifted through hundreds of candidate genes to identify a protein with properties that were suitable for use as a sperm biomarker. One of the qualifiers of the SP-10 protein was that it was found to be highly soluble, so it would quickly diffuse into solutions where it could be measured.

Other milestones along the way had to be passed:

- To be successful as a biomarker, the protein had to be immunogenic—and monoclonal antibody reagents that bound to SP-10 with high affinity required cloning and purifying. A platform suitable for incorporating these antibodies had to be assembled.
- The research team needed to find a method to release the SP-10 protein from its intracellular site within the sperm's acrosome with detergents in a way that would not interfere with the reagents used to assay the protein.
- The need arose to develop a pipette that would uniformly and accurately sample viscous semen.

In the end, the SP-10 protein possessed just the right set of properties for an analyte that could be measured in semen and used to quantify the sperm numbers, or measure fertility in a male. From there, it was a matter of fully developing a commercial procedure, a test kit that could be easily performed in a home setting without too many steps.

In Conclusion

SpermCheck Fertility began as an idea from two of UVA's own: a urologist and a scientist. Of course, from idea to fruition, a lengthy process was necessary, and so we must reemphasize that this story represents an excellent example of the public benefits of sustained NIH investment in basic research.

The research team began with the characterization of a previously unknown gene in the human genome and progressed through a university start-up formation, partnering with a device manufacturer for prototype development, carrying forward preclinical and clinical testing, engaging with and achieving FDA approval for a commercially-marketed product. This bench-to-bedside research also is a fine example of where a university wisely protected its intellectual property rights through patent prosecution.

Ultimately, the beneficiaries are many: men and women in their private lives, clinical medical practice, and the local and national economy. But perhaps the chief benefit is the model that this achievement embodies, the sustained belief that the “virtuous cycle” can be realized, and that the social process of innovation, collaboration, investment, and production can indeed lead to a brighter and more prosperous future.