

Editorial

## Keratoconus: *In Vitro* and *In Vivo*

Karamichos D\*

\*Corresponding author: Dr. Dimitrios Karamichos, Ph.D., Department of Ophthalmology, University of Oklahoma Health Sciences Center, 608

Stanton L. Young Blvd, DMEI PA-409, Oklahoma City, OK 73104; Tel: 405-271-4019; Email: [dimitrios-karamichos@ouhsc.edu](mailto:dimitrios-karamichos@ouhsc.edu)

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Keratoconus (KC) is a degenerative disease of the front part of the eye, named cornea. KC has three major characteristics: 1) cornea thinning, 2) corneal bulging, and 3) corneal scarring. KC usually appears during puberty and can quickly progress to severe stages leading to blindness. Worldwide 1:2000 people are affected with more prominence in the South Asians, Eastern Mediterranean and North African populations. Despite significant efforts by corneal researchers, the pathophysiology of the disease is still unknown, due in part to the absence of an animal model that can replicate KC.

Studies have considered a variety of factors such as environment and genetics, but the exact cause remains unknown [1-7]. Even at the early stages of the disease clinicians are struggling to diagnose KC due to the fact that is easily confused with severe astigmatism. Patients suffering from KC will experience minor blurring of the vision at the early stages. As the disease progresses, vision deteriorates, sometimes rapidly. Advanced KC patients will experience vision problems such as poor night vision, sensitivity to bright light, "ghost images", and itching of the eye to mention a few.

The latest and probably the most promising clinical approach to KC disease is collagen cross-linking with riboflavin (or CXL). This procedure is relatively easy, quick, and so far it seems to arrest KC progression. Briefly, the surgeon will apply one-time riboflavin solution to the eye with the defect and then illuminate it with UV-A light for 30 minutes to activate the riboflavin [9, 10]. This process strengthens collagen bonds in the stromal area of the cornea and restores some of the cornea's mechanical strength.

This cross-linking technique was introduced in Europe about 10 years and is now used clinically to treat KC patients. In the USA, CXL is currently in clinical trials and is expected to be approved by the FDA for clinical use in the near future. CXL is normally used following removal of the epithelium layer to ensure riboflavin penetration into the stromal layer. In 2004 [11], scientists attempted the

the technique leaving the epithelium intact and the results have been promising. Since then, there has been an ongoing scientific "argument" over whether the epithelium should or should not be removed. Several studies have recently been published on this issue and even the duration of UV-A exposure is now questioned by scientists [12]. The reality is that we do not have long-term clinical data in our hands for either of these variables that allow us to determine which works best. In fact, CXL as a technique in general is very young and we do not know whether this stops the KC progression once and for all. Does KC re-appear sometime in the future? If it does, can we redo the CXL? Is it safe? Can the corneal stroma withstand it? These are just a few of many questions that need to be answered in the future.

In an attempt to answer some of these questions scientists are trying in vitro experiments using cadaver eyes from donors and are testing the effectiveness of riboflavin and its penetration [13]. It is clear that in vitro experiments are needed not only to further describe the effects of CXL, but also to understand cellular and molecular mechanisms of cells isolated from KC donors versus normal individuals. In 2012 [14]. We published the first 3D in vitro model which allows human corneal cells from KC donors as well as healthy individuals to secrete and assemble their own extracellular matrix (ECM). This has provided us with a key tool for the investigation of these cells in their natural environment (i.e. ECM). Others have also published work on KC stromal cells mainly looking into conventional 2D cell cultures. Overall, these studies are very important if we are going to understand the molecular mechanism behind the KC defects.

In summary KC is a multifactorial disease and a variety of factors must be considered if we ever going to understand its development and progression. Clearly, huge advancements have been made over the last ten years, both clinically and scientifically but we need further and greater understanding of the molecular events that lead to KC before we can effectively treat it.

### Conflict of interest

No financial interest or conflict of interest exists.

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