Celebrating Commencement

On June 2, 2016, SKMC Dean Mark Tykocinski, MD, shared the following comments with graduates at Jefferson's 192nd commencement ceremony. His remarks appear here in lieu of his usual column.

This year, I visited Japan for the first time—a country with deep historical ties to Jefferson. Among many highlights, I met with one of the luminaries of Japan's medical community, and an honorary degree recipient here onstage: Dr. Fumimaro Takaku.

Putting myself in a Japan mindset, I embraced the writings of Haruki Murakami, one of Japan's most distinguished literary writers and a winner of the Jerusalem Prize for the Freedom of the Individual in Society. His novels are as much poetry as narrative. In his masterpiece novel *1Q84*, which I just finished, he writes: "Where there is light, there must be shadow, where there is shadow there must be light. There is no shadow without light and no light without shadow."

This motif resonated instantly for me, triggering my graduation message to you: seeing, deeply seeing, enhancing one's ability to see the light beyond the shadow.

Class of 2016: Four years of medical school have afforded you an ability to see what others might not, to observe nuances in patient histories, to pick up on subtle situational cues. My call to you now is to take your seeing skills to the limit.

I'd like to suggest three ways to enhance your seeing. First, make the most of your innate seeing capacity—that with which you've been endowed and is embodied within you. Next, feel free to borrow lines of sight from others. And third, avail yourself of the marvels of design and engineering that dramatically extend the seeing capacity of us all. To capture this notion of "enhanced" or "deeper" seeing, I look, metaphorically, to the *fourth cone*. Let me explain.

The timing of my Japan journey could not have been more perfect. The magnificent autumn foliage in Kyoto was at its peak—a sea of color that dazzled. So let's start with color. How do you and I register colors?

Most of us are *trichromatic*—"tri" because our retinas are packed with three distinct types of color-sensitive cells, or cones, each tuned to one of three color wavelengths. Mixed and matched, they yield a rainbow of colors.

Interestingly, some women in this hall trump the rest of us, big time, in their visual capacity. Genetic roulette has endowed the lucky ones with a fourth retinal cone, tuned to yet a fourth color wavelength band—made possible by an X chromosome-linked genetic variant of the color-detecting protein, opsin. This fourth retinal cone enables astonishingly rich color perception—an ability to see a staggering spectrum of 100 million distinct shades, as compared to just one million for the rest of us mere mortals.

You *tetrachromatic* women, with four independent channels for conveying color information, see an incredibly rich color tapestry that escapes the rest of us run-of-the-mill three-cone types. This is your take-it-for-granted normal state. You can see what the rest of us can't see. As one tetrachromatic artist described: "Even the dullest pebble on the road shimmers like a kaleidoscope."

But there's a fascinating twist here. The fourth opsin variant is actually not that rare. If so, why is it that only a small subset of women with it can actually see in vastly greater Technicolor? While the gene variant is a prerequisite, it is not enough. Translating this potential into actual demands "color training." Only a few women with the fourth opsin gene actualize this potential.

Graduates, your training has armed you with a metaphoric fourth cone, now "factory-installed" by us, in your DNA—making it possible for you to see what others can't. But this is just latent potential. Like the opsin gene variant, it must be honed and requires a willingness to absorb, conceptually and practically, what your eyes take in. Whether it is the dimensionality of your patients' lives, or intricacies of complex clinical data sets, aim to see and absorb all that is before you.

You can enhance your seeing potential in a way that draws beyond yourself. For this, I've crafted a second seeing metaphor—what I'll dub the "borrowed camera."

At a dean's concert this year, a lead jazz performer shared an interesting tidbit about his band's CD's cover photo. The photographer, Roza Zah, never uses his own camera. Instead, this homeless man, living in the shadows, only uses borrowed cameras. This anecdote instantly clicked. Enhanced seeing is not just about cultivation of your own retinal cones, but about co-opting the cones of others. From borrowed cones come new vistas.

In a sense, this is simply a matter of seeing things afresh. A recent breakthrough in cancer therapeutics is illustrative. Take Bortezomib, branded Velcade—a first-in-class proteasome inhibitor considered a breakthrough treatment for multiple myeloma. It was originally designed for muscle-wasting diseases such as AIDS and muscular dystrophy. The logic: inhibit the proteasome, the cell's garbage disposal, and thereby slow inadvertent chewing up of normal muscle.

Mark L. Tykocinski, MD
Provost, Thomas Jefferson University
Anthony F. and Gertrude M. DePalma Dean, Sidney Kimmel Medical College

That application never did materialize. But Avram Hershko, an Israeli chemist who would later win a Nobel Prize for his work on cellular waste disposal, suggested the team turn its attention to cancer instead. He argued that by curbing the proteasome's appetite, Bortezomib might prevent the destruction of key proteins in the beneficial immune cells that repel cancer. They took his suggestion. They borrowed Hershko's camera, re-tasked the drug and thereby gave birth to a mainstay treatment for myeloma.

The upshot? Be open-minded, willing to cast a broad net and to buck standard narratives. Permit yourselves to see through the eyes of others. Borrow their cameras—their retinal cones.

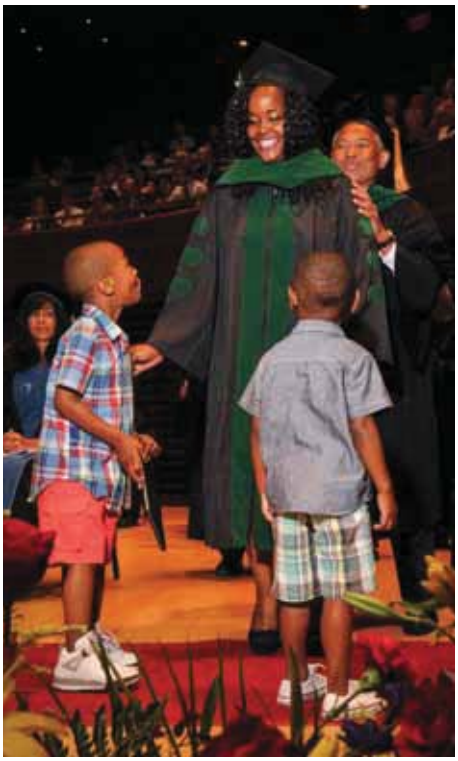
Not all cones are embodied in your eyes or the eyes of others. Yet a third way to enhance your seeing is through artificial, man-made, technologically crafted cones—add-ons, if you will. Twenty-first century mankind is equipped with an astounding set of *artificial cones* to extend our vision and peer into the depths of our universe.

Graduates, this past year—as you were intently absorbed in your hunt for residencies and as the rest of us were distracted by images of terror from Paris and Brussels, horrific civil wars across the Middle East and puzzling election primaries—shadows casting a pall on

us—artificial fourth cones catalyzed a landmark year for mankind's intellectual history. This is not hyperbole. Artificial cones allowed us to see the unimaginable and to send mankind's understanding of the world into hyper-drive. We were amazed. Excited. Bewildered.

I recognize that this is a graduation of a medical college, but the examples of artificial fourth cones from this truly historic "year of the impossible" are especially wondrous in the realm of astrophysics, and so I draw heavily on them here:

- First, in the feats of spacecraft: NASA's *New Horizons* hurtled through space over three billion miles for nine and a half years, offering up the marvels of distant Pluto, at the edge of our solar system, with out-of-this-world images of sights such as massive nitrogen ice-flows. And NASA's *Cassini*, probing Enceladus, one of Saturn's 60 moons, provided mind-boggling evidence of a globe-encircling ocean that accounts for the 101 towering jets of frozen mist erupting from that moon's surface. This salty interior ocean is laced with carbon-containing compounds, making it the most promising extra-terrestrial environment yet in which to search for a second genesis of life.
- And from spacecraft to observatories: This past year, a remarkable artificial fourth cone—the *Hubble* space telescope—allowed us to peer into the far edges of the universe to reveal the most distant galaxy yet, GN-z11. The light from GN-z11 took 13.4 billion years to reach us, meaning *Hubble* allowed us to glimpse the very beginnings of our cosmic history.
- But if there were a Fourth Cone of the Year Award, it would go, hands down, to *LIGO*—the *Laser Interferometer Gravitational-Wave Observatory*, which opened a vast new window on the cosmos. *LIGO*, a stupefying experimental design of bouncing lights and suspended mirrors, enabled a team of scientists to see a burst of gravitational waves from space that originated from a collision between two black holes over a billion light years away.



Amazingly, these are the very gravitational waves Einstein predicted in his general theory of relativity 100 years ago. So *LIGO*—a triumph of quantum optics and a celebration of human ingenuity and engineering, confirmed one of the most profound scientific theories of all time. This powerful fourth cone may someday allow us to see gravitational waves from the Big Bang and to so gaze at the very origins of our home universe.

Of course, this does not even touch on the uber-fourth cone of physics, the *Large Hadron Collider*, which shook particle physics this year when it confirmed the existence of a quantum particle that calculations had long predicted but had eluded the experimentalists—the Higgs boson. This discovery instantly explained why some particles have mass and verified what had been the last unverified and elusive part of the Standard Model of particle physics.

Yes, this is all astrophysics—but the impact of artificial fourth cones has been no less groundbreaking in our realm of life sciences. This year, artificial fourth cones in paleontology and anthropology have started to trace, in unprecedented ways, the origins of *Homo sapiens*. But even more stunning, through gene editing and futuristic technologies that hard-wire electronics into our bodies—for example, brain-machine interfaces that have enabled people to control prosthetic limbs, or smart tattoos composed of implantable skin meshes of computer fibers that can monitor your body's inner workings—we now peer at the awesome prospect of being a species that can direct its own

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further evolution. Our DNA morphed, our biological systems augmented by electro-mechanical ones—a transformation of our species. At once, designers and designed. We can now peer into our past, see into our own inner workings, and we will eventually come to see how we see.

I urge you to draw a sense of optimism from all these artificial fourth cones, to embrace the marvels and beauty they reveal and to appreciate the wondrous things that envelop us—in people and nature. Take all the light in and, in so doing, elevate yourselves, both professionally and personally.

This certainly resonates with Murakami's call for balance between shadow and light. How we see the world is our prerogative. Yes, we see the negative, but we can choose to concentrate our seeing on the world's wonders, its light—with eyes wide open, undistracted by shadow. *Where there is shadow, there is light.*

In closing, my messages to you, Class of 2016:

- Be tetrachromats. Cultivate the fourth cones that are embodied within you—the genetically endowed ones, along with those you incorporate through study. Keep honing your ability to see the world in its richest possible tapestry, its subtleties, its nuances of coloration.
- Do not limit yourselves to your own retinal cones. Borrow the diverse array of retinal cones of others—metaphorically, borrow cameras. Force yourselves to register what others register, be open to diverse perspectives—a kind of seeing that will afford you a lifetime of discovery about people, nature, concepts—and about yourselves.
- Open yourselves up to the artificial cones of 21st century engineering and design, which reveal new vistas and amplify what we can all see. Observe and engage in mankind's wondrous intellectual journey, which allows all of us to see deeper and further, and to see the previously unseen.
- Lastly, it's not just about your seeing abilities; it's as much about what you choose to see. See with optimism. You are fortunate to be launching your professional careers at a remarkable moment in the human journey—a time when our understanding of the world around us shines in Technicolor, a time when the incredible becomes credible. Grant free admission to the diversity and best of mankind, to the light beyond the shadows, realizing that you, in particular, are in the catbird's seat, given your highly cultivated scientific and humanistic grounding. You are a privileged generation. Take advantage of that privilege.

Again, Haruki Murakami crystallizes this thought: "Unclose your mind. You are not a prisoner. You are a bird in flight, searching the skies for dreams."

As you now take the sacred Oath of Hippocrates, permit yourselves to see, like birds in flight, searching the skies for dreams. Hear the profession's ancient call to service, heed its admonitions and affirm your commitment to others, in the most professional and altruistic ways.