Where did you grow up?
I grew up in Namagiripettai, a small town in Tamil Nadu, a southern state in India.

When did your interest in science begin? What was your first experience of science?
I was a first-generation college student, and I did not grow up thinking about science. Until the globalization of the Indian economy diversified job opportunities in India, the school education in India was formulaic and pretty much geared toward making doctors (medical, veterinary, and dental, arguably in that order) and engineers. Following the modus operandi of doing well both in high school (academically) and on a standardized test for admission to professional schools, I joined the Madras Veterinary College to become a veterinarian. During my first couple of years in veterinary school, I learned a lot about basic sciences such as physiology, biochemistry, and microbiology. After transitioning to the clinical segment of my veterinary medical education, it did not take much for me to realize that clinical practice was not my cup of tea! I was much more curious about fundamental biological principles and pathophysiological processes. So I decided to go to graduate school in the US.

That meant taking another standardized test, the GRE, which was unsettling for two reasons: the verbal component of GRE requiring English language proficiency and the cost. Complaining about “what doing well on the GRE has to do with one’s success in graduate school” was a regular topic of conversation among many of us who wanted to do a PhD in the US at that time. Almost two decades later, it is good to see a serious debate on the reliability of the GRE as a predictor of graduate school success and many graduate programs reconsidering GRE as a requirement. In any case, I did not do well on the GRE (in the verbal part, of course). I failed to secure admission to a PhD program, perhaps due to my low GRE score and a lack of any serious research experience. This was a stressful time, as I had to make up my mind about what I wanted to do. With my parents’ backing, I decided to do a master’s program in India to gain more research experience and prepare more for the GRE. After the master’s program, with a much improved GRE score on the retake, my second attempt at gaining admission to a PhD program in the US was successful.

Where and with whom have you studied (undergraduate, graduate, postdoc)?
I joined an interdisciplinary graduate program, Comparative Medicine and Integrative Biology, at Michigan State University, and I did my PhD research in the laboratory of Dr. Linda Mansfield. The Mansfield laboratory was working on an enteric bacterium, Campylobacter jejuni. Much of the work in the laboratory focused on developing mouse models for C. jejuni infection and understanding bacterial virulence mechanisms. Linda was brave enough to ask me to come up with a research project on my own. It took me a while to figure out a research topic that was interesting to me, and eventually I decided to study the host–pathogen interaction during C. jejuni infection in the context of dendritic cells. Since this project was entirely different from anything going on in the laboratory, everything had to be set up from scratch, involving a lot of troubleshooting, and I just loved it. My dissertation work demonstrated C. jejuni–induced activation of dendritic cells, the mechanisms involved, and its impact on T cell activation.

As I wanted to delve deeper into the molecular basis of innate immune recognition of microbes, I joined Dr. Kate Fitzgerald’s laboratory at the University of Massachusetts Medical School—a place to be for innate immunity research—for my postdoctoral training. I consider this a turning point in my career. If there is a checklist of qualities of an ideal postdoc mentor, Kate...
Vijay Rathinam: Cherishing the small victories

Houston Journal of Experimental Medicine

in 2014.

matory cell death response are exciting to me.

during bacterial infections (Rathinam et al.,
quent work identi

tious and in

standing the innate immune basis of infec-

I have a long-standing interest in under-

What is up next for you?

What are you currently working on?

What interested you about your current

area of study?

Innate immune sensing is central to the ac-
tivation of the host immune response. A diverse
set of germline-encoded receptors surveys
nearly all cellular compartments for the
presence of pathogens and their products.
Such compartmentalized surveillance of micro-
bial products has emerged as a key strategy
by which the innate immune system gauges
the severity of a microbial threat and mounts
commensurate defense responses. I am fasci-
nated by an emerging array of pattern rec-
ognition receptors in the cytosol and how they
sense intracellular invasion of pathogens. I
find the host’s differential reactions to intracel-
lar vs. extracellular sensing of pathogens in-
triguing. Particularly, inflammasome-mediated
sensing of pathogens and the ensuing inflam-
matory cell death response are exciting to me.

What are you currently working on?
What is up next for you?

I have a long-standing interest in under-
standing the innate immune basis of infec-
tious and inflammatory diseases. Our work

aims at decoding fundamental mechanisms in intracellular innate immune recognition
and signaling during bacterial and viral in-
fec tions. My laboratory currently works on
cytosolic sensing of bacterial LPS. It has
been known for a long time that TLR4 is the
innate immune receptor for LPS. Surpris-
ingly, we learned in the past few years about
the existence of a TLR4-independent sensing
of LPS that gains access to the cytosol by
a family of inflammatory caspases such as
caspase-11 in rodents and caspase-4 and
caspase-5 in humans. Remarkably, the host
response to LPS in the cytosol is character-
ized by an inflammatory and lytic form of
cell death and IL-1 activation (Rathinam
et al., 2019).

As the subcellular site of LPS sensing
dictates how the host responds, we be-
came interested in understanding how
LPS attains access to the cytosol. My
laboratory recently discovered that outer
membrane vesicles (OMVs), bona fide
secretory vesicles released by Gram-
negative bacteria, act as the vehicle that
mediates the cytosolic localization of
LPS. OMVs activate the cytosolic LPS
sensing pathway, leading to pyroptosis
and caspase-1 activation (Vanaja et al.,
2016). Demonstrating a necessary role
for OMVs for intracellular LPS release
during bacterial infections, genetic atten-
tuation of bacterial OMV production
diminishes their ability to activate
caspase-11-dependent cell death and
IL-1 responses. This work provided key
mechanistic insights into a previously
unknown yet critical upstream event in
the cytosolic LPS sensing pathway. Cur-
rently, our group is working on various
molecular and cellular aspects of cytosolic
LPS sensing and its implications for host
defense and inflammation. The expanding
number of immune surveillance pathways
in the cytosol does not operate in a vac-
uum, and in fact, more than one pathway is
simultaneously engaged during infection
with live pathogens. In this context, an
additional focus of my laboratory is on the
cross-talk among these different surveil-
ance mechanisms in the cytosol and what
that means for host defense at the whole
organism level (Banerjee et al., 2018;
Rathinam et al., 2010). Inflammasome-based
host responses have been implicated in
a variety of human diseases including but
not limited to sepsis, atherosclerosis, and
neurodegenerative disorders. Therefore,
expanding our understanding of inflammasome
signaling events at the molecular level could
potentially reveal new targets for the therape-
utic management of the above described
diseases.

What did you learn during your PhD and
postdoc that helped prepare you for
being a group leader? What were you
unprepared for?

I was fortunate to have supportive PhD and
postdoc mentors who had faith in my re-
search potential and provided me the free-
dom to explore my research ideas. What I
learned during my postdoc years, scientifi-
cally and otherwise, laid the foundation for
me to be an independent investigator. Ad-
ditionally, the whole biological system per-
spective that I gained from my veterinary
medical training provided me with unique
insights into intriguing biological problems.
Together, these training components made
me better prepared scientifically to lead a
research group. However, there are a lot of
skills that you learn as you go; among which,
I would point out a few: developing research
ideas for grants and grant writing, priori-
tizing research projects of interest on the
basis of scientific and practical reasons, as
well as recruiting talented individuals to the
laboratory and mentoring them.

What has been the biggest challenge in
your career so far?

I would say every step of my career was a
challenge in its own way. Having said that,
I regard something related as a main chal-
lenge: my better half, Sivapriya Kailasan
Vanaja, whom I met during my master’s in
India, is also a scientist and has her own
laboratory at the UConn Health School of
Medicine. Finding two PhD, postdoctoral,
and finally tenure-track faculty positions at
the same institutions—without compromis-
ing each other’s scientific interests and
ambitions—was our biggest challenge so far.

What hobbies do you have?

I love photography. Though the time avail-
able for this has dried up lately, I make an
effort to do some photography on vaca-
tions and during my travels for scientific
meetings (one more perk for going to
meetings in great places). Currently, I am
building up my portfolio to do a photog-
raphy exhibit someday. I am also an audio
enthusiast and avid cricket fan—no surprise there for the latter, for someone who grew up in India.

Any tips for a successful research career?
Research is a challenging but rewarding career. With the caveat of “easier said than done,” I would say some of the qualities that enhance the odds of being successful in research are passion, perseverance, resilience, and the courage to go beyond one’s comfort zone. Research is teamwork, and developing that skill right from the beginning can only help. Also, I would emphasis for prospective doctoral and postdoctoral trainees that it is important to find the right laboratory and mentor that would be compatible and suitable for their professional interests, short- and long-term. Finally, to borrow from the inspiring writing of Dr. Ron Vale (Vale, 2019), enjoy the basic discovery and cherish small victories!

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