Resiliency of a perpetual optimist: neurosurgeon Dr. Linda Liao

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It is not possible to capture all the depth that composes Dr. Linda Liao: chair of the Neurosurgery Department at the University of California, Los Angeles; second woman to chair a neurosurgery program in the United States; first woman to chair the American Board of Neurological Surgery; first woman president of the Western Neurosurgical Society; and one of only a handful of neurosurgeons elected to the National Academy of Medicine. Her childhood and family history alone could fascinate several chapters of her life's biography. Nonetheless, this brief biography hopes to capture the challenges, triumphs, cultural norms, and spirit that have shaped Dr. Liao's experience as a successful leader, scientist, and neurosurgeon. This is a rare story. It describes the rise of not only an immigrant within neurosurgery—not unlike other giants in the field, Drs. Robert Spetzler, Jacques Marcos, Ossama Al-Mefty, and a handful of other contemporaries—but also another type of minority in neurosurgery: a woman.

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EVEN among the highly select group of people that compose the neurosurgical community, Dr. Linda M. Liao stands out as an incredible anomaly. To those with limited insight into neurosurgery, she is a walking contradiction: small in stature and introverted by nature. But look closer and she is also a leader among leaders in the field, who paved a path for herself that few have before. Equal parts intelligent and humble, she found an identity within the profession that is uniquely her own.

Now the chair of the Department of Neurosurgery at the David Geffen School of Medicine at the University of California, Los Angeles (UCLA), Dr. Liao is only the second woman, and the first Asian American woman, in the United States to chair an academic neurosurgical department (2017).¹ To this day, in 2020, there have been only four female chairs of neurosurgery programs in the US. Dr. Liao has held many titles as the first woman: chair of the American Board of Neurological Surgery (ABNS) (2019–2020),² president of the Western Neurosurgical Society (2015–2016), editor-in-chief of the *Journal of Neuro-Oncology* (2007–2017), elected member of The Society of Neurological Surgeons (2013)³ and the National Academy of Medicine (NAM) (2018),^{4,5} and countless other leadership and scientific accolades. She is a wild success by any standards.

Sitting across from Dr. Liao at a table, one sees her

calmness and candor shining through, as well as her youthful glow; years of neurosurgery do not seem to have worn her down. There is a spark in her eye. She speaks in a reassuring, easy tone that one presumes her mother used even after a long day in the labor factories of downtown Los Angeles. This is Dr. Linda Liao's story.

Part 1: Childhood

Dr. Liao's mother, Sue Hong-Tsu Liao, came from a family of merchants. Sue's mother (Linda's grandmother) was born one of 9 girls into a wealthy Taiwanese family before the Chinese Communist revolution. Three of the girls were exchanged for an adopted brother, who acquired the family name and family inheritance. The women in the family inherited nothing; girls were viewed as a liability to be given as dowry to a future husband.

Customary for the time, at the age of 21 years, Linda's mother was offered to her father, John Ta-Lang Liao, in an arranged marriage in the town of Tainan in southern Taiwan. Shortly after they were married, John emigrated to the US to attend graduate school at Case Western Reserve University. Sue, who spoke no English, traveled to the US to join John and, returning to Taiwan pregnant, gave birth to a daughter. Linda Liao was born in Tainan, Taiwan, in 1967 (Fig. 1).

ABBREVIATIONS ABNS = American Board of Neurological Surgery; GBM = glioblastoma; NAM = National Academy of Medicine; NIH = National Institutes of Health; PI = principal investigator; UCLA = University of California, Los Angeles.

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Although her father studied in the US prior to her birth, Linda grew up in a decidedly traditional Taiwanese household, deeply entrenched with many gender disparities. She muses that her father likely had always wanted a boy, though he ended up with two girls, Linda and her younger sister, Anna, now a lawyer, who was born in Springfield, Ohio, following her mother's return to the US. Linda recalls little of her childhood in Ohio except for the sideways glances or gawks she and her family received at the neighborhood Kmart. Revisiting childhood photographs, she reflects that she seemed to be the only non-Caucasian in her preschool classes.

When Linda was 5 years old, her parents moved their young family to Magnolia Avenue by the present-day University of Southern California. The area was decidedly inner-city and poor. Her family continued to be a recognizable minority among primarily Black and Hispanic neighbors. She attended the still-standing 32nd Street Elementary School, a public school with few resources at the time. In the third grade, her parents were able to secure her a spot at St. Vincent's School (a predominantly Hispanic, Catholic school in downtown Los Angeles)—despite not being Catholic—with hopes for better educational resources.

Her parents valued education and did their best to provide for their daughters during their humble beginnings. Her father worked toward a real estate license, and her mother worked long hours at the equivalent of various sweat shops in downtown Los Angeles. Her mother held many odd jobs, one as a seamstress, which became Dr. Liao's first job as a child. She earned a few cents per article of clothing by stringing up laces on women's garments that her mother had brought home to work on.

Her mother in particular supported Linda's academic success. Sue had only completed high school and had not been given a chance to pursue higher education. Before she married, Sue's fate in life was to tend the modest family stall at the swap meet in their small hometown in Tainan, selling knick-knacks and wrinkled plums. Meanwhile, Sue's family's resources had been allocated to her three brothers: one became a doctor, one inherited the family stall at the swap meet, and one became a schoolteacher. Sue always envied her physician brother; it was her dream to pursue a career in medicine. Instead, her brother lived out her dream. He attended medical school, residency in New York, and moved back to Taiwan as a head and neck surgeon. Sue wanted more for her daughters than had been available to her.

A gifted child in math and science, Linda would soon be able to chart her own course in life, even without the resources that her parents could not offer her. By the fifth grade she had intellectually outgrown the material taught in class. She was unexpectedly pulled from classes for 3 days for a barrage of psychological and IQ tests by the school guidance counselor. Shortly thereafter, she was placed directly into seventh grade at a new college-prep school that was recruiting gifted students, Whitney High School, on which the book *School of Dreams: Making the Grade at a Top American High School* (2003) is based. By this time, her mother had started working as a bank teller and her father had earned his real estate license. Though

FIG. 1. Family photograph of Dr. Linda Liao, younger than 1 year of age, in Tainan, Taiwan, 1967, with her mother, Sue Hong-Tsu Liao. Copyright Linda Liao. Published with permission.

still struggling to make ends meet, they were now better able to support her junior and high school education in another city, so the family moved to Cerritos, California.

Linda's early academic prowess and internal drive were evident, thereafter earning her acceptance to a variety of nationally prestigious academic programs. But, despite all her accomplishments to date, Dr. Liao states that her mother remains the smartest person she has ever known.

Part 2: Education

Her mother's words of constant encouragement, and her dream of being a physician to help people, lingered in Linda's mind when she moved 3000 miles away at the age of 16 years to Brown University's 7-year medical education program. During her undergraduate years, she majored in biochemistry and political science. Still in need of monetary support for her education, she arrived at Brown on work study. She found a job in a laboratory cleaning glassware. Her relentless curiosity and intellectual drive soon got the best of her, and she could not help but inquire about the work the postdoctorates were doing in the laboratory. Not long after, the laboratory principal investigator (PI), Dr. Jean M. Marshall, began involving the inquisitive young Linda in a variety of laboratory projects. The research focused on gastrointestinal motility, but Linda was singularly fascinated by the role of the nervous system in this complex process. Dr. Marshall began to invest in Linda's education and helped her complete her honors thesis in preparation for medical school. Although she could have stayed at Brown, Linda was tired of the weather and desperately homesick to return to California. Her laser focus on research drew her to the heavy-hitting academic neuroscience research centers. She graduated from Brown

in 1987 and then attended Stanford University School of Medicine (1987–1991).

Upon arrival at Stanford, the budding scientist contacted a variety of neuroscience professors and heard back from neurology professor Dr. Stephen J. Peroutka. Linda's technical laboratory skills blossomed, and, despite her PI leaving academia for a job in industry partway through her training, she had enough data to publish her first paper on the characterization of a novel serotonin (5-HT_{1A}) antagonist, which was a pindolol derivative affectionately called “Lindalol” in the laboratory. She lightheartedly says she should have been studying serotonin agonists; it would have made her a fortune in a time before Prozac, which is now widely used for depression. But like most things in her life, she takes this in stride. One gets the sense that, despite her proclivity for goal setting and achieving, maybe she is driven most by the thrill of the intellectual journey.

Perhaps the only major setback in life that she felt wholly ill-equipped to deal with was the passing of her mother in 1994 after a 15-year struggle with breast cancer. With her mother's worsening health and her PI having left Stanford, instead of completing her PhD through the National Institutes of Health (NIH)–funded Medical Scientist Training Program for the development of physician-scientists, she was convinced by her mother's looming mortality that she needed to “get on with life” and find a way back to Los Angeles to care for her. Linda returned to clinical rotations her 3rd year of medical school. Carrying her deeply rooted interest in neuroscience through her rotations, she could not identify with the hands-off feel of neurology, and felt a slow personal descent after rotating on a locked psychiatric ward with severely affected patients. She rotated on neurosurgery last and found a perfect fit, her sense of wonder again peaked.

On this rotation, Linda met Dr. Frances Conley, the first woman to be granted a tenured professorship in neurosurgery at a US medical school (1982), and first to be a full professor of neurosurgery (1986). Dr. Conley was both physically and intellectually impressive as an avid runner and javelin thrower, and a female general and spinal neurosurgeon who operated alongside all-male colleagues. She was also an early pioneer of the concept of harnessing the immune system, specifically by introducing bacteria (i.e., *Corynebacterium parvum*) into a tumor cavity to induce an immune reaction to potentially treat glioblastoma (GBM), which was thought of as a hopeless death sentence at the time. This was a radical idea for the time, potentially inspiring some of the groundwork for Linda's later research on brain tumor vaccines and immunotherapy.

Dr. Conley, along with attendings such as Drs. Gary Steinberg, Larry Schuer, and John Adler (inventor of the CyberKnife), supported Dr. Liau as she pursued her passion for neurosurgery while a medical student at Stanford. She sought out UCLA as a perfect fit for residency; it not only brought her back “home” to Los Angeles to be near her ailing mother but also was famous for research in traumatic brain injury under the leadership of Dr. Donald Becker. She saw an opportunity to start research in the field of identifying biomarkers and new treatments for head trauma and brain injury.

FIG. 2. Dr. Linda Liau graduating from Stanford Medical School, 1991. Copyright Linda Liau. Published with permission.

In 1991, she graduated from Stanford Medical School (Fig. 2) and started neurosurgery residency at UCLA (Fig. 3). Though physically closer to her mother, Dr. Liau now lacked time to devote to Sue's care. Her sister, Anna, took their mother to doctor appointment after doctor appointment. The family struggled to get Sue into a clinical trial for Herceptin, which was not yet FDA approved. By the time Sue's care was transferred to UCLA oncologists Drs. John Glaspy and Dennis Slamon (who developed Herceptin), her cancer had widely metastasized, including to her brain. When Dr. Liau's mother passed during her 4th year of residency, she experienced the greatest regret and guilt of her life: that she had been unable to spend more time caring for her mother in those final days.

Ever trying to make sense of the insensible, Dr. Liau drastically shifted her intellectual and research efforts toward oncology. The year her mother died, she entered the fledgling UCLA Specialty Training and Advanced Research (STAR) Program, allowing her to pursue a PhD degree during residency/fellowship, which she completed in 1999. That same year, she received an NIH K08 grant under the mentorship of Dr. James Economou (her mother's surgical oncologist), applying the principles of immunotherapy for melanomas and carcinomas to cancers of the brain, specifically GBMs. He would go on to be her academic mentor throughout her professional career as a faculty member at UCLA. When Dr. Liau was elected to NAM in 2018, Dr. Economou was at the awards ceremony beaming with pride.

Around the time when Dr. Liau started on faculty at UCLA, her previous mentor, Dr. Fran Conley, still at Stanford, experienced a great setback. Dr. Conley was professionally respected among her male peers, who dominated the specialty at the time. But, having been passed over for

FIG. 3. UCLA neurosurgery residents, 1997. Dr. Linda Liau is pictured in the front row, second from right. Copyright UCLA Department of Neurosurgery. Published with permission.

chairman positions, she authored *Walking Out on the Boys* (1998), chronicling her challenges as a woman in medicine. She lost favor in the neurosurgical community thereafter. But she was 30 years ahead of mainstream culture, and though she was a martyr for the cause of advancing women in medicine, she is now noted as a pivotal catalyst in history books. The professional fall of a prodigious mentor greatly saddened Dr. Liau, but she intended that she too would be a role model someday, if only she made it that far.

FIG. 4. Family photograph (left to right): Dr. Marvin Bergsneider, Bianca Bergsneider, Dr. Linda Liau, and Brandon Bergsneider at the Rose Bowl, June 2019. Copyright Linda Liau. Published with permission.

Part 3: Professional and Adult Life

Dr. Liau is potentially one of the few neurosurgical figures who is simultaneously endowed with all aspects of success. In addition to being a coveted physician-scientist, she is a successful leader, role model, wife, and mother. She is commonly asked how she balances everything, to which she refreshingly and unabashedly responds, “You don’t. You can’t balance it all synchronously, but you can have it all, in parts, at various stages of your life.”

Stage 1: Mother, Scientist

She explains that early in her faculty career, she embarked on her greatest accomplishments to date with the births of her two children, Brandon Bergsneider, born in 1998 (she operated until her water broke in the operating room), and Bianca Bergsneider, born in 2001 (Fig. 4). Her pregnant belly seemed to limit new patient recruitment, so she made the most of her time as a young attending developing her laboratory and research, while being a mother to two young children alongside a husband who was also a busy practicing neurosurgeon. She somehow managed to breastfeed and pump between cases for a year for each of her children; it was not easy. But she smiles as she mentions their names.

With funding from her initial NIH K08 award, she hired Dr. Robert Prins, who had just completed his PhD at the Medical College of Virginia, as her first postdoc, and Sylvia Odesa as her laboratory manager. Dr. Liau seems to be deeply loyal; Dr. Prins now has his own laboratory and is a full professor in the Department of Neurosurgery at UCLA, and Ms. Odesa remains her laboratory manager.

FIG. 5. ABNS 75th Anniversary and Mary Louise Spencer's (executive administrator for the ABNS for almost 30 years; middle of first row, gray dress) retirement party, June 27, 2015. All of the other people in the photograph were current or former ABNS board directors. Dr. Linda Liao is pictured in the front row, third from right. Copyright American Board of Neurological Surgery. Published with permission.

er to this day. In this early phase of her career, Dr. Liao made the seminal discovery that cytotoxic T cells can be activated *in vivo* to traffic into brain tumors, despite the long-held dogma at the time that the brain was “immune-privileged” and devoid of immune reactivity.⁶ By the time she was a 5th-year faculty member, she had already completed the first-in-human treatment of a GBM patient with a dendritic cell (DC) vaccine (1999) and started the first-in-human phase I/II trials of an autologous tumor lysate-pulsed DC vaccine (2003).⁷ She had identified a novel glioma-associated growth factor gene⁸ and developed a new *Listeria* vaccine in animal tumor models.⁹ By the time she was 34 years old, she had earned three NIH R01 grants and an R21, a seemingly impossible academic feat in such a short period of time. As she would say, “the numbers speak for themselves,” and indeed others seemed to agree.

At one of her many national plenary talks about her research, she was approached by the American Association of Neurological Surgeons/Congress of Neurological Surgeons Tumor Joint Section president at that time, Dr. Joseph Piepmeier, and asked if she would be interested in joining the Tumor Section's Executive Committee. Dr. Piepmeier became a mentor to Dr. Liao, and she later succeeded him as the editor-in-chief of the *Journal of Neuro-Oncology*. As she continued to develop her research acumen, she discovered a relationship between cytomegalovirus viral immunity and tumor immunity in GBM patients¹⁰ and was involved in the landmark discovery that cancer-associated *IDH1* mutations produce 2-hydroxyglutarate.¹¹ Because of her groundbreaking research, her notoriety on the national stage grew and leadership opportunities started flooding in, whether for department chair, national board positions

(Fig. 5), journal editorships, or standardizing policies regarding neurosurgical practice.

Stage 2: Clinician, Leader

Having developed a strong basic/translational science foundation, Dr. Liao transitioned into the next stage of her career—a focus on patient care built upon a reverence for life, as she daily encountered GBM patients who had abandoned all hope. There are patients from her early immunotherapy vaccine trials who are now surpassing all odds, living up to 17 years after their deadly diagnosis was made, with phase III trials derived from her initial preclinical discoveries and phase I clinical results currently still ongoing. While she grew her clinical practice, her notoriety allowed her to grow an extended professional network within neurosurgery as well.

She speaks of her patients and neurosurgery colleagues fondly, as if they are extended family. In weaving together the narrative of her life, one starts to understand that she is the kind of person whose talent begets talent, whose relentless curiosity and perhaps joyful obsessiveness with her research engender infectious creativity and thoughtfulness in others.

Stage 3: Role Model, Historical Figure

Three years ago, Dr. Liao transitioned into her third professional stage of life as she took on the role of chair of the Department of Neurosurgery at UCLA (Fig. 6). She also transitioned into a symbol of inspiration nationally. She had accomplished firsts. She had become one for the history books. Her primary goals shifted from singularly

FIG. 6. Dr. Linda Liao (foreground) as chair of the UCLA Department of Neurosurgery (resident and faculty members in the background) on Department Photo Day, July 2017. Copyright UCLA Department of Neurosurgery. Published with permission.

FIG. 7. Dr. Linda Liao and her first female trainees as department chair. **A:** Dr. Linda Liao (*left*) and Dr. Jos'lyn Woodard (*right*), fellow (2020 graduate). **B:** Dr. Jasmine Thum, post graduate year (PGY)–5. **C:** Dr. Sophie Peeters, PGY-4. **D:** Dr. Maya Harary, PGY-2. Copyright Sophie Peeters. Published with permission.

personal research or clinical goals to facilitating the goals of others; shaping residents for their future, enabling other attendings to achieve their goals; and building the department she served.

Deeply humble, she plays off her countless research, clinical, and leadership triumphs as mere kismet, but this volume of achievement cannot be accomplished without sheer grit and determination. Despite being a staunch intellectual, strongly swayed by numbers and statistics, it is clear that she is a deeply optimistic, hopeful individual. She has to be, in order to muster such resiliency for herself and for her patients. Her delightful wonder about the world is reflected in the glimmer in her eyes as she talks about all that she still hopes to accomplish in her already wildly successful career.

Part 4: Parting Wisdom

To merely chronicle the experiences of Dr. Liau's life, the facts and the figures that make her curriculum vitae exceptional, is to overlook the extraordinary human being. Her humility, grace, and empathy, perhaps sometimes to a fault, often prevent those on the outside from truly understanding the daily challenges she must have faced. She was an immigrant and racial minority for most of her childhood, then rose as a star in a profession historically dominated by men.

Though she speaks little of it, one can infer the lifetime of explicit and implicit challenges she has faced, whether because of her race or her gender. Her extreme resilience, whether natural or developed as a coping mechanism to persevere, typifies who she is at her very core. Her sense of self is strong; it had to be to get this far in life and to live up to her strongest female role model, her mother. She is so deeply empathetic that she interprets slights and prejudices against her as a woman in the field as reflective of insecurities or ignorance of the offender. In such cases, Dr. Liau expands pattern recognition and demonstrates that women can excel in the profession. It is with singular insight that one can begin to see how—now in her seat of power, still likely subject to some nonbelievers—she is able to shrug off all that she has endured.

At the top of her field, Dr. Liau serves as a de facto mentor for young women in neurosurgery everywhere (Fig. 7). She always recommends that women medical students interested in neurosurgery talk to current residents; neurosurgery residency has significantly changed in the last 20 years, she says, perhaps with both a wistful and decidedly “as it should be” tone. I sometimes wonder how many volumes her challenging experiences could fill. I wonder how she endured both emotionally and intellectually. But I know she does not give it a second thought. She simply refuses to let the world dictate her life, perhaps as a reflection of her favorite quote:

No one can make you feel inferior without your consent.

— Eleanor Roosevelt

And so she doesn't.

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Disclosures

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