Brain Medicine

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Vicki L. Clifton: Stress, sex, and the placenta: its role in fetal and child development

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Professor Vicki Clifton, PhD, GAICD, Dip Manag, Dip Counselling, FRSM, is a Mater Research Institute-University of Queensland Amplify Fellow specializing in obstetrics research through clinical trials and basic biology. With 327 publications, h-Index: 61, and over 14,000 citations, her research focuses on stress and maternal asthma during pregnancy, examining their effects on maternal health, placental function, fetal growth, and child health. She is notably recognized for her work on sex-specific placental function and stress responses influencing fetal growth and pregnancy outcomes. Professor Clifton has led her institution's asthma and pregnancy research program, establishing multi-disciplinary, end-user-engaged research programs in Australia and overseas. Her innovative research has advanced our understanding of factors affecting asthma during pregnancy, leading to new models of care and improved fetal outcomes. Her work has influenced national and international asthma management guidelines, identified sex-specific mechanisms affecting maternal-fetal health, and expanded the frontiers of existing knowledge on fetal-neonatal physiology. Through preclinical studies and clinical partnerships, she has rapidly translated findings into practice guidelines and consumer information. She currently leads the Queensland Family Cohort study, a state-wide longitudinal study linking parental and child health outcomes to biological mechanisms. A Fellow of the Royal Society of Medicine, she pioneered women's leadership as the first female President of the Endocrine Society of Australia and the first female Editor of Placenta (Elsevier). As an NHMRC Research Fellow (2000-2023), she has secured over \$25 million in category 1 grants. We are privileged to have Professor Clifton share her personal and professional insights with our readers in this Genomic Press Interview.

Part 1: Professor Vicki Clifton - Life and Career

the pivotal moments that first kindled your passion for science?

I was greatly influenced by my parents, grandparents, and great-uncle, who taught me about agriculture, marine life, geology, paleontology, plants for food and medicine, and a bit of chemistry while working in my mum's hairdressing salon and understanding why hair ended up curly with a perm. Science was all around me, and it seemed natural to focus on a science degree. I attended the University of Newcastle and was fortunate to have lecturers and mentors who recognized my potential and guided me into postgraduate study. At the same time as starting my postgraduate research degrees, I had 3 babies, with one of my sons dying in midgestation. This devastating experience led to the question, "What went wrong?" and eventually led to studying the placenta. I joined the Mothers' and Babies Research Centre at the University of Newcastle and started my PhD examining placental circulation and its regulation by stress hor-

mones. Following my PhD, my family and I were keen on an adventure,

Could you give us a glimpse into your personal history, emphasizing



Figure 1. Vicki L. Clifton PhD, GAICD, Dip Manag, Dip Counselling, FRSM, Mater Research Institute-University of Queensland, Australia.

so I accepted a postdoctoral fellowship with Prof John Challis at the University of Toronto. This was my first introduction to fetal physiology and stimulated my curiosity for understanding the mechanisms that regulate placental function and fetal growth and survival.

We would like to know more about your career trajectory leading up to your most relevant leadership role. What defining moments channeled you toward that leadership responsibility?

After living in Canada for my postdoctoral fellowship for two years (1995–97), I returned to the University of Newcastle, Australia, where I started

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to examine the role of maternal asthma and stress and its effect on the placenta and fetus (1998-2007). I formed some key collaborations and established the first controlled asthma and pregnancy birth cohort. However, during this time, my first husband died, and after several years of grieving, supporting my children, and feeling lost, I remarried and decided I needed a fresh start. I was Deputy Director at the Mother's and Babies Research Centre, and I had no foreseeable opportunity to be promoted further and gain further leadership experience, so I started to look for new positions at other institutions. I met the Director of the Robinson Research Institute in Adelaide, who invited me to the University of Adelaide to see what I thought of the city and discuss new leadership opportunities. My partner and I fell in love with Adelaide and decided to move. I was appointed Director of Clinical Research at the Lyell McEwin Hospital in Northern Adelaide as the hospital transitioned to a tertiary-level teaching hospital (2008-2015). It was a great experience developing a strategy for introducing research to the hospital and then engaging clinicians in research activity.

After seven years in Adelaide, I was invited to Brisbane to give a talk at the Mater Research Institute. Mater has the biggest maternity hospital and neonatal intensive care unit in Australia, and I was very impressed with its potential for continuing my research. I was offered a position as Program Leader of Mothers, Babies, and Women's Health at Mater, and although I was not considering a move, the offer was too good to ignore in terms of what I could achieve, and the challenge was intriguing. This exciting new adventure would allow me to establish a large birth cohort in the state and increase my capacity to collaborate with fantastic researchers across several Universities and Institutions.

I follow my intuition on when to make a change in my career, and as a result, I have enjoyed the experience of moving to new jobs and exploring new places. I am still in Brisbane and love my role at the Mater Research Institute. Many of my latest leadership roles include Board Director and Secretary of Women's Health and Equality Queensland. I wanted to contribute to improving the lives of vulnerable women, and donating my time to a not-for-profit organization has been a more tangible way to make a difference in the lives of women. This role has also opened up many other great opportunities, including being a part of the advisory panel that developed the Queensland Government's Women's and Girls Health Strategy. At this stage in my career, I continue to focus on my research and work on my favorite organ, the placenta!

Please share with us what initially piqued your interest in your favorite research or professional focus area

I started working in asthma and pregnancy research due to my own lived experience. I am an asthmatic, and I had severe symptoms during pregnancy which resulted in adverse outcomes for my babies (1989–91). I found that the clinical care for my asthma, specifically during pregnancy, was lacking. A literature search identified that there was very little research in the field. I was fortunate to be co-located with Obstetrics and Respiratory Medicine at the John Hunter Hospital in Newcastle and started to discuss potential projects with Professor Peter Gibson and Professor Warrick Giles. This led to the establishment of the first controlled prospective birth cohort of pregnant women with and without asthma (1999-2007). Since then, the research in this field has expanded exponentially with the establishment of several different birth cohorts, randomized controlled trials, and epidemiological studies that have translated into significant improvements in clinical practice. The work has morphed into examining the effect of stress on the placenta and fetus, which has led to a greater focus on maternal mental health in pregnancy.

What impact do you hope to achieve in your field by focusing on specific research topics?

Based on the evidence from my research, male and female fetuses are physiologically different, which is partly conferred by the placenta's sex-specific function. Presently, we do not consider the sex of the fetus in Obstetrics. I would like to see sex-specific medicine for pregnancy compli-

cations, for the care of preterm neonates, and for the care of newborns. Our work also suggests that maternal physiology in pregnancy varies depending on the sex of the fetus, and I hope the evidence we provide could translate into clinical decisions around interventions for pregnant women based on the sex of the fetus.

Please tell us more about your current scholarly focal points within your chosen field of science

Currently, we are focused on how the placenta may influence maternal stress, anxiety, and depression. We have discovered that the placenta has 13 different isoforms of the glucocorticoid receptor, with one isoform expressed in the presence of maternal stress, anxiety, and depression that activates an inflammatory response in the placenta in the presence of high cortisol concentrations. Most glucocorticoid receptors inhibit inflammation, so this new finding is surprising. This work may explain why high levels of stress and high inflammation can coincide. Increased inflammation in women with anxiety and depression can act directly on numerous parts of the brain to exacerbate symptoms, and we hypothesize the placenta has a role in contributing to the rise in inflammation with pregnancy and, in turn, influencing mum's brain. We are working on the mechanisms right now; maybe this work will impact the management of perinatal mental health somewhere in the future.

What habits and values did you develop during your academic studies or subsequent postdoctoral experiences that you uphold within your research environment?

Say yes as much as you can. Always stay up to date with the literature, invest time weekly in supporting your team and students, stay connected with your wider network, and communicate clearly. Don't be afraid to ask for what you need or take a risk on an idea, and persevere when you fail. Further your education.

At Genomic Press, we prioritize fostering research endeavors based solely on their inherent merit, uninfluenced by geography or the researchers' personal or demographic traits. Are there particular cultural facets within the scientific community that warrant transformative scrutiny, or is there a cause within science that deeply stirs your passions?

Aboriginal and Torres Strait Islander people of Australia deserve equal opportunity in all aspects of society, including science. Greater investment in culturally appropriate school education for Aboriginal and Torres Strait Islander children that leads them to culturally appropriate University education and academic careers is essential for changing the outcomes for this important population. I am especially passionate about improving the lives of Aboriginal and Torres Strait Islander women and seeing them empowered through education.

What do you most enjoy in your capacity as an academic or research leader?

I love the whole job, but there are three aspects of being an academic that I particularly enjoy. First of all, the data! It is a privilege to think about a problem, formulate a hypothesis, and test it. Second, working with different people locally, nationally, and internationally who have different areas of expertise and think differently from me. Third, and most importantly, being able to mentor and supervise students.

Outside professional confines, how do you prefer to allocate your leisure moments, or conversely, in what manner would you envision spending these moments given a choice?

I have an amazing husband, a circle of close friends, and a beautiful family, and most of my free time is spent with them. If I had nothing else going on, I would probably snorkel on the Great Barrier Reef every day. I regret not being a marine biologist some days. Maybe I will do another PhD in marine biology when I retire!





Figure 2. Vicki Clifton and her partner snorkeling on the Great Barrier Reef near Cairns. She reflected on her first reef experience: "We were on an organized tour, and it was a silly tourist picture. However, it makes me smile whenever I look at it because it was an amazing day."

Part 2: Professor Vicki Clifton - Selected questions from the Proust Ouestionnaire¹

What is your idea of perfect happiness? A healthy family is living their best life.

What is your greatest fear? Climate change.

Which living person do you most admire?

Many people. Senator Linda Burney, Jane Goodall, and Greta Thunberg.

What is your greatest extravagance? Long holidays.

What are you most proud of? My family.

What is your greatest regret?

Not speaking up when I knew something was wrong and not following my intuition when I knew it was right.

What is the quality you most admire in people? Fearlessness.

 $^{1}\mbox{In}$ the late nineteenth century, various questionnaires were a popular diversion designed to discover new things about old friends. What is now known as the 35question Proust Questionnaire became famous after Marcel Proust's answers to these questions were found and published posthumously. Proust answered the questions twice, at ages 14 and 20. In 2003, Proust's handwritten answers were auctioned off for \$130,000. Multiple other historical and contemporary figures have answered the Proust Questionnaire, including among others Karl Marx, Oscar Wilde, Arthur Conan Doyle, Fernando Pessoa, Stéphane Mallarmé, Paul Cézanne, Vladimir Nabokov, Kazuo Ishiguro, Catherine Deneuve, Sophia Loren, Gina Lollobrigida, Gloria Steinem, Pelé, Valentino, Yoko Ono, Elton John, Martin Scorsese, Pedro Almodóvar, Richard Branson, Jimmy Carter, David Chang, Spike Lee, Hugh Jackman, and Zendaya. The Proust Questionnaire is often used to interview celebrities: the idea is that by answering these questions, an individual will reveal his or her true nature. We have condensed the Proust Questionnaire by reducing the number of questions and slightly rewording some. These curated questions provide insights into the individual's inner world, ranging from notions of happiness and fear to aspirations and inspirations.

What is the trait you most dislike in people? Ignorance.

What do you consider the most overrated virtue?

Cleanliness: I despise housework and thrive in creative clutter.

What is your favorite occupation (or activity)? Snorkeling.

Where would you most like to live?

I already live there: by the ocean in Australia.

What is your most treasured possession?

A cedar bedside cabinet carved by my Great Uncle Peter for my Great Aunty Ciss when they were engaged about 110 years ago. Their love and respect for each other was inspirational.

When and where were you happiest? And why were you so happy then? I did not realize it was my happiest day until I looked back and found it was never like that again. My closest family and friends, whom I love dearly, were all together at my second wedding. It was a great celebration by the ocean, with the sun shining and the conversation, laughter, food, and wine flowing freely. Since then, I have lost many of my family members to illness, accidents, and aging, so that day will never be recaptured.

What is your current state of mind?

Content but motivated.

What is your most marked characteristic? Loyalty.

Among your talents, which one(s) give(s) you a competitive edge? Creativity and perseverance.

What do you consider your greatest achievement?

Translating my research into a tangible outcome for women's health.

If you could change one thing about yourself, what would it be? Doubt in my ability.

What do you most value in your friends? Loyalty.

Who are your favorite writers?

William Kotzwinkle and Anita Diamant.

Who are your heroes of fiction?

Ayla in Clan of the Cave Bear by Jean Auels.

Who are your heroes in real life?

Captain Paul Watson and Julian Assange.

What aphorism or motto best encapsulates your life philosophy? Carpe diem.²

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²Latin phrase meaning "seize the day" – a call to make the most of the present moment rather than waiting for tomorrow.



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