

# The roots of accomplishment

From a New Jersey beauty parlour to cutting-edge genetics by way of her own alopecia, Angela Christiano's life has all been tied up with hair. **Helen Pearson** meets a woman whose head is full of the stuff that covers it.

**N**o one forgets their first encounter with Angela Christiano. For Jorge Frank, it was in an office at New York's Columbia University in 1995. "In walks this blizzard of a woman with the bright smile and the big hair and these long fingernails," recalls Frank, a molecular dermatologist at University Hospital Maastricht in the Netherlands. "I thought: 'This is a rock star not a scientist'."

Christiano certainly cuts an arresting figure. Deep-brown and bronze tresses erupt from her head in a gravity-defying explosion and surge over her shoulders. Her perfect make-up and carefully manicured nails complete an image that is the antithesis of a stereotypical scientist.

But for Christiano, hair is not just an adornment. It is a filament that binds together her appearance, her family, her personal life and her work. Descended from two generations of hairdressers, she came to appreciate hair's true importance when her own locks began to fall out in an episode of alopecia areata. Working at Columbia, she immediately shifted the focus of her research from skin disease to hunting down the genes that underlie human hair disorders, such as an atavistic condition in which people sprout thick hair all over their faces. Her scientific work may even end up with a cosmetic use, saving men and women with normal but nevertheless unwanted hair from shaving, waxing and depilation.

## Grooming talent

Christiano grew up in New Jersey with an unusual appreciation for the importance of personal grooming. Hair and nails — "ectodermal appendages", as she now calls them — were her family's bread and butter. Her grandparents had set up a barber's shop after immigrating from Italy; her mother worked as a hairdresser and beautician. Christiano spent after-school hours sweeping up hair in her mother's shop. "I didn't realize it at the time," she says, "but I was becoming a keen observer."

Many of her schoolmates went on to become hairdressers and beauticians, and Christiano's family expected her to stay at home until she



**Ectodermal appendages:** Angela Christiano leads a research life that is shaped by hair.

got married. But by that time, school had already kindled in her a love for genetics, and she was the first of her family to attend college and earn a PhD, at Rutgers University in New Jersey. She didn't abandon her roots though. Having watched so many hours of beautification, she found herself drawn to dermatology. "It is one of the only areas in medicine where visual things provide clues," she says. "Once I was exposed to a skin disease it was like instant love."

The subject is rarely the focus of such enthusiasm; indeed, dermatology is sometimes given short shrift in medicine. Very few dermatological conditions are life threatening, and a concern with unsightly skin or hair can be dismissed as vanity. As a result, those working in the field take great pains to spell out the

difficulties faced by those with alopecia and other disorders. "Every day I have someone in my clinic crying and saying they want to commit suicide," says Abraham Zlotogorski, a specialist in hair disorders at Hadassah University Medical Center in Jerusalem, Israel, and a collaborator of Christiano's.

Christiano established herself in the science of skin during her postdoctoral position at Thomas Jefferson University in Philadelphia, Pennsylvania. While there, she studied the genes underlying epidermolysis bullosa — a condition in which the skin is incredibly fragile, blisters and falls off, and one of very few life-threatening skin diseases.

## First signs

When she was 30, Christiano had just started a faculty position at Columbia, and felt under pressure to establish her own group in dermatology. Then one day, her hairdresser in New Jersey asked her whether she'd had a biopsy: "You have a little spot." The next day, a colleague who worked across the hall took a closer look and

let out "the most blood-curdling scream I've ever heard", Christiano recalls. The spot was the size of an orange. In her new apartment, the blocked shower that she had attributed to bad Manhattan drains turned out to contain a clump of her hair.

Christiano was diagnosed with alopecia areata, a disease in which the immune system attacks hair follicles, causing hair to fall out in patches, or sometimes completely. Because the stem cells in the follicles escape the attack, the hair sometimes grows back, and the condition can come and go throughout life. Christiano had known that

hair problems ran in her family: her mother and grandmother both developed female pattern baldness and wore wigs. Now she learned that a distant cousin had a more severe form of

**"Every day I have someone in my clinic saying they want to commit suicide." — Abraham Zlotogorski**

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alopecia areata and did not have any hair at all.

As soon as she was diagnosed, she decided to refocus her work on alopecia. Alopecia areata is known to involve several genes and is hard to trace through families. But Christiano found a Pakistani family in the scientific literature who had a simple, inherited form of alopecia called papular atrichia. The gene involved causes a specific phenotype in which babies lose their first hair from the front of the head to the back and then remain bald.

By looking for genetic landmarks inherited alongside the condition, Christiano's team narrowed its search for the responsible gene to a large region of chromosome 8. But the group was not able to narrow it down any further until Christiano attended a meeting of the Society for Investigative Dermatology and heard a talk about a mutant mouse called hairless that also loses its hair in a wave from head to tail. The human equivalent to the gene turned out to sit on that suspicious section of chromosome 8, and when she sequenced it in her Pakistani patients, they all had mutations that seem to prevent hair growth and destroy the hair follicle<sup>1</sup>.

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### From mice to men

Since then, Christiano has tracked down genes in two other hair disorders in a similar way, using human families alongside mouse models. In one disorder, she showed that a type of cadherin, a protein that holds cells together in the hair follicle, is mutated in people whose hair breaks off near the head like razor stubble<sup>2</sup>. With time, the gene hunting has become easier, thanks to human sequence data and high-resolution genome maps. Last year, she and her colleagues took only six weeks to show that some families who had no nails on any of their fingers or toes had a mutation in a gene normally active in the embryo's developing nails<sup>3</sup>.

Christiano is sensitive to the accusation that she is merely 'stamp collecting' — bagging genes for the sake of it — and tries to delve into what each gene does and how they drive skin and hair development. But she admits that the



Hypertrichosis (above) and alopecia areata both have genetic underpinnings.

hunt has an addictive rush: "It's one of the most exciting things we do. When we have a new gene, it's like having a new baby." And it's not as if all gene hunting is now easy. One of Christiano's most intractable puzzles is in her "Mexican hair people", who have thick, 'terminal' hair all over their faces rather than the finer 'vellus' hair, which is normal. Christiano and her team have spent more than five years studying one of the only reported cases of a family with this disorder — called hypertrichosis<sup>4</sup>. But although they sequenced 82 genes in the relevant region of the X chromosome and every snippet of microRNA, they could not find a causative mutation. Some kind of genetic trickery could be afoot: perhaps a mutated RNA outside the protein-coding genes is failing to regulate a gene on another chromosome.

To her obvious delight, last year Christiano made headway in the genetics of her own affliction. Various researchers have identified families in which several members have the disease, and Christiano and her collaborators have been able to pinpoint four locations in the genome that are strongly associated with the condition in these families<sup>5</sup>. If they find the actual genes, they might be able to unravel the immune system's antipathy to hair follicles, and

even suggest ways that drugs could abate it.

Christiano had hoped that a company called Sirna Therapeutics, which is based in San Francisco, would find a use for her discoveries. Sirna had licensed some of the patents from her work and, before the company was acquired by Merck in late 2006, researchers with the company were trying to find a way to deliver inhibitory RNA to the skin to curb hair growth, with an eye to the cosmetic market. Despite her background and impeccable grooming, Christiano says that she is not interested in developing cosmetic applications from her work. She wants the company to find a way to deliver the inhibitory RNA to the skin so that she and other researchers can use it to hinder genes involved in conditions such as alopecia.

Her own case didn't need such interventions. Over two years she lost ten large patches of hair and became obsessed with her tresses, checking them constantly and

carefully styling and dyeing them to hide the nude spots. But her hair came back, although with an odd, wiry texture. "Now every day I have hair, it's like an accomplishment."

The flamboyance of her accomplishment with her ectodermal appendages can lead to some teasing. When she goes to conferences that have hairdryer-free accommodation:

"I have to bring my entire arsenal, and people make fun of my luggage." The teasing may, on occasion, give way to unfair criticism, says skin researcher Elaine Fuchs of Rockefeller University in New York: "Some scientists tend to judge people by their scientific pedigree and their appearance, and Christiano doesn't fit the mould."

"What I so admire about Christiano [is that] she proves these people wrong by her accomplishments." And Fuchs isn't talking about that hair. "I've learned that it's a phenotype really," Christiano says. "Everyone has a phenotype and this just happens to be mine."

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Mice provided some clues for tracking down genes involved in human hair disorders.

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