one learns in such settings is how familiar task of learning how to attack a genetic disease directly at the level of the underlying defect, J. Seegmiller by using gene therapy – in other words, introducing foreign genes into cells that were unable to function normally. By serendipity and fate, I was doing post-doctoral training in several of the laboratories that were spearheading these techniques, including the Nobel Prize laboratories of Renato Dulbecco at the Salk Institute, and Fredrick Sanger in Cambridge, England.

The revolutionary advances in molecular biology and genetics over the past half-century are producing amazing changes in how we understand and treat human disease. One of these is what is called gene therapy, and it came to birth at UCSD. As medical science has come to understand that most human disease results from a combination of genetic defects and environmental factors, therapy has been undertaken either by addressing the physiological and metabolic effects of abnormal genes or by altering environmental influences. This is usually done by prescribing drugs (or in the case of lung diseases, by persuading people not to smoke cigarettes). For instance, type I diabetes, which results from mutations in the genetic machinery that regulates insulin production and function, is treated not by correcting the underlying genetic defects but rather by simply adding more insulin. Similarly, other diseases such as cystic fibrosis and hemophilia are treated not by correcting the responsible genes themselves but rather by using drugs or functional additives—in CF to ameliorate or prevent the symptoms of disease; in hemophilia, by replacing the clotting protein product that is missing because of the underlying gene defects.

By Theodore Friedmann
Professor of Pediatrics

The birth of molecular biology in the 1960s and 1970s brought unprecedented new powers not only to sort out exactly how genetic changes cause disease but also to purify genes, to determine their structure and sequence, and to introduce them into human cells to replace missing or abnormal functions in the cells. By serendipity and fate, I was doing post-doctoral training in several of the laboratories that were spearheading these techniques, including the Nobel Prize laboratories of Fredrick Sanger in Cambridge, England, and Renato Dulbecco at the Salk Institute. What
really relevant outside of laboratory curiosity. Some vocal religious groups thought it arrogant and unacceptable human folly to want to alter human genetics, even in the cause of relieving suffering. But science advanced and the design of clinical trials improved, and by 2002 the first truly convincing clinical success was reported in the gene therapy of a genetic form of immunodeficiency in children—the so-called “bubble boy” disease. Shortly after that came astounding results with Leber’s Amaurosis, a form of retinal disease that causes progressive visual deterioration and blindness. In the past several years, all these successes have been achieved with clinical trials of gene therapy for hemophilia, several childhood neurodegenerative disease, and other metabolic diseases. 

As impressive as these advances have been with these relatively rare single gene diseases, even more remarkable have been several recent advances that have taken gene therapy into the realm of much more common and complex multi-gene diseases such as forms of cancer. In a technology that has come to be called CAR-T cancer immunogene therapy, the T cells in the blood that have failed in their surveillance responsibility to detect and prevent the emergence of cancer cells have been re-programmed by gene therapy methods to recognize, seek out and destroy leukemia and other cancer cells. The technology is astounding and even in its current early developmental stage is certain to become a gold-standard form of combined immune and gene therapy for a growing number of cancers.

These forms of gene therapy are based on the concept that disease prevention and therapy can be achieved by leaving the defective genetic material ---

Instead of showing my regret, I simply say the rule’s all wet. For principle I’m pledged to fight With all my potency and might. The one I hold most high and right is: “Keep my course load good and light.” I know the stuff will not complain If I am careful to refrain From asking that they all disdain Those month-long leaves in France and Sparrk

And who cares what the students say—

Let them protest in any way, If three-ninths of my summer pay is covered by the C-I-A

When chancellors and provosts ask That I perform some boring task, I pack my opaque sleeping mask

And head down to the beach and back. In short in ruling o’er my lair By sitting on my derriere I am the very model of a modern departmental chair.

Committees are my heart’s delight, So I appoimt ‘em left and right. They put my critics out of sight And keep them busy day and night. When CAPE reports are not so hot, I’d like to see the students shot. Instead they say ‘they’re high on pot Or victims of a right-wing plot. My Penner Formula’s precise, My Chair’s Reports are most concise I make decisions in a trice, And sell my soul at any price. The budgetary winds may blow— And other salaries go low— Because of all the dirt I know, I’ll always get my quid pro quo

If I were shown a deanery, I wouldn’t like the scenery. I’d rather run machinery, Or even try a beanery. In short in ruling o’er my lair By sitting on my derriere I am the very model Of a U-C departmental chair!

By Sandy LaRoff

It’s probably true, as the saying goes, that nostalgia isn’t what it used to be, but I still remember fondly the La Jollywood Revue produced by Connie Mullin Bronscomb in 1998 (and a year later I think), with Harold Ticho, Stan Chodorow and Joe Watson doing “Three Little Deans from School Are We” and Ralph Levins’s clever number lamenting that while other schools had acronyms like “sunny, cal, or mit,” ours abbreviate to “ucsd.” And when there was my bit which I hope you will find worth repeating:

(To the tune of “A Derry Air”)

I am the very model of a modern departmental chair. My rule my lair with perfect fair By sitting on my derriere. My faculty and staff don’t care That I alone their worth compare; They know the running I prepare Are never less than fully fair. Recruitment is compatible With action affirmative And credits for subbilatonic Are strictly mathematical. When I propose an appointee, The file I send to C-A-P Is always filled from A to Z With ludicrous hyperbole! Administrators are my guide, And when my colleagues say they’ve lied, I always try to save their hide, And pin the blame on Systemwide. In short in ruling o’er my lair By sitting on my derriere I am the very model Of a modern departmental chair.

I never need to fuss or fret When Senate rules I do forget;
caught in a quizical pose, not surprised or flirtatious but smart, sly, the most alive being in that scene. How tremendous to have a pretty mother! Except for her quick pose the bodies in the scene are oblivious to the camera, involved in the every-day, the ordinary, but they too are now included. What roots this in the moment and makes it typical is the two shadow-heads at the bottom, the silliness of that mistake of framing, with the person holding the camera unintentionally included in the shot. The perfect image of my mother, before she was married and my mother, advances through and beyond all that surrounds her. We could crop all the rest, but that would violate history and the wonderful imperfection that snapping a shot requires.

When I see this I hear all the coming story, taking it out, at the last, to another scene in my scansion, where my nephew wades into a spring pool in the Colorado mountains to mingle my mother’s ashes with my father’s ashes, swirling them together in the snowmelt. That is for me, because snapshots are not for strangers. Strangers will tell their own stories.

By Donald Wesling
Professor Emeritus of English Literature

Eight banker’s boxes in the garage contain over three thousand photos. Some were ripped from the pages of scrap-books with glue and remnants of black pages stuck to the back, so the images on the front were slowly disappearing. These were pre-digital, mostly pre-phone camera photos from the early 20th century to yesterday. Eras and persons, covering five generations of German-Irish Weslings and Ukrainian-Norwegian Dulinawkas, were entirely scrambled.

The task was to preserve and organize, so that eventually we’ll have copies of a DVD with slide-shows set to music, to give to children and grandchildren. Since my wife Judith disagrees with my categories, thinks my plan hasty and restricted, I waited until she went to Wisconsin for a visit so I could set out piles of pictures on tables in the living room.

In my seventy-sixth summer, I set out to organize these into fourteen categories starting with the life-stories of my wife and myself as founders of our little clan, working through our three children, six grandchildren, our own parents on both sides, places we’ve been, documents that deserve to be kept. (Documents include children’s drawings, home-made New Year cards and a copy of an honorary doctorate from Budapest.) My two rules of selection were to spare embarrassment for all of us: No Pictures of Naked Children; No Pictures of Old Boyfriends/Girlfriends. It was wrong to admit these exclusions to Judith, who’s horrified by my obscuring of the total record. But the one who does the work gets to make the rules!

We inherited the old black-and-white photos from our parents: scenes from their thirty-to-fifties Buffalo, from Judith’s family farm south of Buffalo, from my parents’ summer cabin on Rice Lake. The silliness of that mistake of framing, with the person holding the camera unintentionally included in the shot. The perfect image of my mother, before she was married and my mother, advances through and beyond all that surrounds her. We could crop all the rest, but that would violate history and the wonderful imperfection that snapping a shot requires.

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Lake in Canada. We ourselves took almost all of the rest. After about 1970, all photos are in color. Certain patterns of family recording only emerge when I do my survey: first child of two or three always receives eager photographic attention, later children less so; after a child hits thirteen or fourteen, hardly any photos can be found, so plausibly they're using them.

What is the meaning of photo-graphs for the art that captures memories by the action of light on sensitive surfaces, for the life of the one quickly caught, the catcher, the viewer? What do we have in family photos that may be different from news or portrait photos, different from professional artistic or documented work? The scanner would answer that the snapshot has most intimacy to do with living in a once-only space and time, living in family, living in community. The snatched moment at the dinner table, on the front porch or back deck, the child ren on bikes, the egg-hunt, wedding rehearsal, funerals, funerals, boys flashing rabbit-ears behind the heads of brothers, views of a collapsed barn. Snapshots are random and raw, unpracticed, and yet the photos of everyone, even babies, have in the face a guarded awareness, the intelligency of permission. Head-on there is always an element of self-contained amazement. I see this not only in humans but in cats, too. The only exception to this comes when the camera catches a face from the side, a head from the back.

For most of us, not continually on show like actors, it’s only through the family snapshots that we see our first portraits on the side or back, our height in relation to other, what happens to our eyes when we hold a toddler who’s our child or our child’s child. We are actors continually on show, but we forget that for long stretches.

Seeing all my beloved human family who are alive while I am alive, tracking each of them through a hundred or more photos of different stages of their lives, I realize vividly through images what I knew in theory, that the body is the mind and the face is the feelings and the words taken or mirroring the office of West Seneca’s historical society. Our fathers carried lunch-pails; they punched a card in a clock at arrival at the Chevy Plant or Bethlehem Steel. Their generation was the last massively to move from working middle-class, because they could enjoy decent sales and pensions.

A distortion like a physical rage takes over the middle-school child in the years twelve to fourteen—years of orthodonture, unly new long hair, acne, suddenly long limbs, black hoods worn every day of the week, reluctance to be photographed. Out of this is emerging the young adult fifteen of the eighteen whose body is increas-ingly achieved, in gestures of un-speakable grace, skin with ruddy-golden glow, foxy-faced, careless sexually ready, caught in sociable stride or in a bikini at a beach party, girls and boys both nearly beyond those terms, on the edge of independence, never again so beautiful but not knowing that.

Your mid-life twenties, thirties, forties, fifties, sixties, all those busy years rush past so eagerly, so momentarily, that the images can’t be dated. The seventies to the nineties are known in their ravages, so we would speak only of how the face would smile, accept the humiliation of the rot-ten image as the price of partic-ipating, caring and being cared for, so good sports we, all of us, are. We’re only surprised that we’re not surprised at understanding this about our parents, whose head-of-closet photos Judith and I and our siblings have now long since taken on.

Our parents lived from the second decade of the twentieth cen-tury to the first decade of the twenty-first. They experienced the Depression, World War II, dads working in Buffalo factories and mothers working cleaning other people’s homes or minding the office of West Seneca’s historical society. Our fathers carried lunch-pails; they punched a card in a clock at arrival at the Chevy Plant or Bethlehem Steel. Their generation was the last massively to move from working middle-class, because they could enjoy decent sales and pensions.

The photos show that from early on both families had their own rural retreats, forty acres with a cabin and Christmas trees for Judith’s family, and a cabin-plus-duck pond on Rice Lake in Canada for my parents’ long summer of fishing, after retirement. High-school graduates who came to a life of work in the last years of the Depression, they sent all of us to college in the fifties when tuition was $2,000 a year. That seems low, but to place that number in perspective, consider that of those years the Wesling house in South Buffalo cost all of seven grand.

Photos show that our par-ents were often at gatherings in halls of fire-stations, churches, cabins and open-end shelters at local parks, their own homes or homes extended to include beers in ice-bucket, card-games, story-telling, dancing. They were often out in restaurants for fish-fries or beef-on-weck. My parents had Canadian friends for fishing, boating, or staying up half the night to play cards. Unlike Judith and me, who used our salary to travel for study, jobs, other countries, my parents had no get-out-of-town longings. They had parties with the people around them. They could talk all night engaged, razor sharp.

They knew how to have fun. Now we, helped by these images, are the only ones who remember the achievements, joys, and sufferings of that generation. That’s one thing I’ve come to know, scanning the family photos. I knew it already but now I know it more massively across the two thousand images, each of which takes a minute in the Epson scanner. I know it in detail through these snaps, which are more trustworthy as evidence exactly because they’ve been scanned and scanned and scanned. And no conceivable record could be complete.

I also know better these things I already knew: the horror of nameless emotions that rush past a smile, the proud welcome of a little boy’s weight in his mother’s arms, the wild urgency of the search to repro-duce, the hard-wired sequence of the body’s changes from a baby girl’s fat little feet to veils like worms in her great-grandmother’s arms.

Writers already knew what I now know from them and from my scanning. Samuel Johnson in his essay on biography said: What is nearest us touches us most. Robert Frost in his poem on being a swinger-down of birch trees said: Earth’s the right place for love---I don’t know where it’s likely to go better. Yes, Frost, and photography, a technology now ancient and vanishing and requiring scan-ning to stay, is in the family snap-shot transforming love, light, and earth into meaning.
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Coda: What I Did in Practice; Example Photos

The Editor has encouraged me to add a Note on how I performed the scanning. This is a large un-dertaking, with expense of money and time. Others may be like me and put it off several years. It may encourage you to scan your photos if you know more or less exactly what it takes.

To begin, I made fourteen family photo categories (categories will be different with each family, but I will say this: I focused on Judith and me as founders of a little dynasty, put first and then went to our chil-dren, their children, our four par-ents, and a few other things). I sorted the eight boxes containing 3000 photos into these categories in large manila envelopes, ending up with 2000 in folders and 1000 left aside as redundant, bad, in-convenient.

I purchased an Epson scanner for about $100, and got the more expensive version with capability to scan negatives (this feature I never used). I set the scanner on my computer table so I could lift the top of the machine to place each photo with out leaving my chair. Scanning thousands of pages, not per-sonally individually is a dreary, repet-itive process. Therefore the ac-tion—Turn On computer and scan-ner, Greet Scanner, Lift Lid, Place Photo, Close Lid, Click to Scan, Wait 45 seconds for Scanner to hum and grumble through the scanning, use Mouse to Place New Image in Correct Folder; Lift, Place, Remove Photo—needs to be made as automatic as possible so you can think of other things while it is happening.

Getting from the eight boxes and the fourteen large envelopes to the end of scanning took six weeks, probably working about fifteen hours a week. I did not realize that unless I did nobody

the ever would, but grudging every minute.

I made two mistakes that affected the whole of the final product: not being chronologi-cally accurate in the mid-life photos of all my family members, and wrongly aligning oversize items so they appear 90-degrees side-ways instead of straight (affecting perhaps 5.0% of complete set of images).

But what I accomplished was something like a multi-per-son, century-long saga, the story of a family, actually many families, through images. Scan-ning, in this instance, turned out to be story-telling. My secret mission was to make something happen in the future: to break some grandson’s heart in twenty or thirty years when he sees the story in the middle of our lives.

The whole project, saved on a flash-drive an inch long, took me to a copy company in Clairemont Mesa so they could record on master-DVDs, with flashing of each image for five seconds, and with an overlay of music from a young fifteen-year-old, Lionel Hampton that I supplied. This cost $200.

Included here is my favorite photo of all I surveyed, as exam-ple. I did not know how to scan it and cannot do. It is the best I can offer, both because it carries so much affection, so much story, but also because it exemplifies the whole genre. In the fore-ground is Helene Marguerite Bullinger Wel singly, my moth-er, youngest child of a family of eight, immigrant Germans in South Buffalo; in the back-ground her very old parents (my younger now than the grandparents I have as the sister’s children. It is the mid-1930s, she is probably 17, she is
caught in a quizzical pose, not surprised or flirtatious but smart, sly, the most alive being in that scene. How tremendous to have a pretty mother!

Except for her quick pose the bodies in the scene are oblivious to the camera, involved in the everyday, the ordinary, but they too are now included. What roots this in the moment and makes it typical is the two shadow-heads at the bottom, the silliness of that mistake of framing, with the person holding the camera unintentionally included in the shot. The perfect image of my mother, before she was married and my mother, advances through and beyond all that surrounds her. We could crop all the rest, but that would violate history and the wonderful imperfection that snapping a shot requires.

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CHRONICLES JANUARY 2016 PAGE 6

A new initiative launched in 2014, the UCSD Emeriti Association now has a Book Club, which meets from 12 noon to 2 p.m., on the fourth Monday of each month at the Ida & Cecil Green Faculty Club. The next meeting will be held on Monday, January 25th. The book to be discussed will be: “Jonas Salk: A Life by Charlotte Jacobs”.

The following meeting will be held on Monday, February 22. The book to be discussed will be “A Question of Honor, Kosciusko Squadron: Forgotten Heroes of World War II” by Lynne Olson and Stanley Cloud.

Please RSVP on the EA RSVP website: https://hrweb.ucsd.edu/ea/

By Donald Wesling Professor Emeritus of English Literature

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We inherited the old black-and-white photos from our parents: scenes from their thirty-to-fifties Buffalo, from Judith’s family farm south of Buffalo, from my parents’ summer cabin on Rice Lake. We are at an unprecedented and enormously optimistic time for gene therapy. Many universities, research institutes, and private pharmaceutical and biotechnology companies are moving with great speed to implement these stunning new techniques. However, despite the fact that the field of gene therapy was born in the exciting and innovative biomedical cauldron of UCSD and the general La Jolla scientific community, UCSD, ironically and very sadly, has not yet committed resources to enable this university to resume its role as a world leader in developing this exciting new and explosively growing area of science and medicine and in delivering the benefits of gene therapy to patients in hospitals and clinics at UCSD and around the world. We owe this amazing technology to our patients and, as the birthplace of gene therapy, we at UCSD should be among those at the forefront of its brilliantly promising advance.

An SNP (“typo” or “spelling mistake”) is a change of a nucleotide at a single base-pair location on DNA.
showed that we could correct the abnormal function responsible for the terrible childhood neurological condition known as Lesch-Nyhan disease by exposing the cells to normal DNA. This very debilitating genetic disease was first described clinically by yet another physician/scientist – William Nyhan -- who came to the newly established UCSD School of Medicine as the founding chairman of the Pediatrics Department.

But the genetic correction we managed to achieve in the Sengmiller lab was very inefficient. It was obvious that we would need to develop much better methods to introduce specific foreign genes into human cells. I supposed that could be achieved by using engineered and “disarmed” versions of the agents in nature that perform this specific function as their normal job description – viruses. The need to figure out how to disable the usually dangerous tumor viruses and use them as gene transfer agents brought me to Dulbecco’s lab at the Salk. I hoped to learn how to remove the disease-causing genes of the virus and replace them with potentially therapeutic genes for highly efficient transfer into human cells. My bench-mate in the laboratory, Richard Roblin, and I first used the phrase “gene therapy” to describe such a use of genetic material as a therapeutic agent to correct a genetic defect underlying a human disease.

After additional postdoctoral training with Sanger in Cambridge, I was finally armed with the tools to isolate the human HPRT gene responsible for Lesch-Nyhan disease. (HPRT stands for nothing less daunting to the uninitiated than hypoxanthine guanine phosphoribosyltransferase!) Working with Inder Verma and other colleagues at the Salk, my group and I succeeded in inserting the purified gene into virus particles and demonstrated that infecting HPRT-deficient cells with such a virus -- a gene transfer “vector” -- corrected the genetic and functional defects in the cells.

That was proof of principle that a normal copy of a gene delivered by an engineered and disabled virus vector could reverse the metabolic and biochemical damage responsible for a human disease. At the heart of this first experimental proof of principle of gene therapy was Lesch-Nyhan disease. Its genetic mutation was first identified by Sengmiller and the responsible gene was first isolated and sequenced by my laboratory. Nyhan, Sengmiller, and I were or later became members of the UCSD medical faculty. Gene therapy was thus born here in La Jolla and was made possible by our colleagues’ obsessive interest in this rare but fascinating genetic disease.

The application of this new technology to human beings was at first unsuccessful and aroused criticism. Clinical trials of gene therapy in patients with genetic disease were first undertaken in 1989-1990 with very immature technology. The efforts were beset by scientific and medical setbacks, improper and inadequate clinical design, and even ethical lapses. These setbacks lent support to some of the early suspicions about the feasibility and propriety of gene therapy. Some scientists considered the goal to be unachievable and not really relevant outside of laboratory curiosity. Some vocal religious groups thought it arrogant and unacceptable human folly to want to alter human genetics, even in the cause of relieving suffering. But science advanced and the design of clinical trials improved, and by 2002 the first truly convincing clinical success was reported in the gene therapy of a genetic form of immunodeficiency in children -- the so-called “bubble boy” disease. Shortly after that came astounding results with Leber’s Amaurosis, a form of retinal disease that causes progressive visual deterioration and blindness. In the past several years, additional successes have been achieved with clinical trials of gene therapy for hemophilia, several childhood neurodegenerative disease, and other metabolic diseases. As impressive as these advances have been with these relatively rare single gene diseases, even more remarkable have been several recent advances that have taken gene therapy into the realm of much more common and complex multi-gene diseases such as forms of cancer. In a technology that has come to be called CAR-T cancer immunogen therapy, the T cells in the blood that have failed in their surveillance responsibility to detect and prevent the emergence of cancer cells have been re-instructed by gene therapy methods to recognize, seek out and destroy leukemia and other cancer cells. The technology is astounding and even in its current early developmental stage is certain to become a gold-standard form of combined immune and gene therapy for a growing number of cancers. These forms of gene therapy are based on the concept that disease prevention and therapy can be achieved by leaving the defective genetic material unaltered.

Instead of showing my regret, I simply say the rule’s all wet. For principle I’m pledged to fight With all my potency and might The one I hold most high and right is: “Keep my course load good and light.”

I know the staff will not complain If I am careful to refrain From asking that they all disdain Those month-long leaves in France and Spain. And who cares what the students say— Let them protest in any way, If three-ninths of my summer pay Is covered by the C-I-A! When chancellors and provosts ask That I perform some boring task, I pack my opaque sleeping mask And head down to the beach and back. In short in ruling o’er my lair By sitting on my derriere I am the very model of a modern departmental chair. Committees are my heart’s delight, So I appoint ‘em left and right. They put my critics out of sight And keep them busy day and night. When CAPE reports are not so hot, I’d like to see the students shot. Instead they say they’re high on pot Or victims of a right-wing plot. My Pennen Formula’s precise, My Chair’s Reports are most concise I make a decision in a trice, And sell my soul at any price. The budgetary winds may blow, And other salaries go low— Because of all the dirt I know, I’ll always get my quid pro quo

If I were a deanery, I wouldn’t like the scenery. I’d rather run machinery, Or even try a beanery. In short in ruling o’er my lair By sitting on my derriere I am the very model Of a U-3 departmental chair!
Mark your calendar for 2016 events!

Richard C. Atkinson, UC President Emeritus and UCSD Chancellor Emeritus  
Topic: “The history of UCSD and the UC System from his unique perspective.” To see what he has talked and written about in recent years, visit his website: www.rca.ucsd.edu.  
Wednesday, February 10, 2016, 3:30 - 5 PM  
Ida & Cecil Green Faculty Club

Steven Schick, Reed Family Presidential Chair in Music, a percussionist, conductor, author and distinguished professor of music.  
Topic: “Learning to Conduct Lesson #1: Understanding Sound and Silence”  
Wednesday, March 9, 2016, 3:30 - 5 PM  
Prebys Music Center Concert Hall