PXE Awareness

National Association for Pseudoxanthoma Elasticum (NAPE, Inc.)

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A Season for Hope

National Association for Pseudoxanthoma Elasticum (NAPE, Inc.)

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President's Message


Dr. Frances Benham

Dear NAPE Friends,

Recently Lydia Chang, NAPE member from New York, reminded me that when we first met at a NAPE annual conference some seven years ago PXE patients faced a gloomy future. We recalled remarkable changes since that meeting. Dr. Ken Neldner had announced the study to find our mutant gene and many NAPE members became study participants. Remember our excitement when Dr. Berthold Struk announced his finding of the locus of that gene? Three other labs joined him in the sprint to identify it and all did just that in the same week several years later. NAPE rejoiced with a grand celebration at our conference that year.

Photodynamic Therapy was another cause for hope, which probably was a bit over-blown as we so wanted a cure. Soon Macugen followed and was approved by the FDA and Medicare. Genentech announced its finding that VEGF (vascular endothelial growth factor) created conditions in the eye for the development of leaky blood vessels in neovascularization which unchecked leads to retinal scarring and central vision loss. Genentech's Avastin, a fragment of its cancer treatment, inhibits VEGF and saves some vision. Genentech then announced Lucentis, now approved by the FDA and Medicare as a VEGF binder or

inhibitor which also appears to protect vision. And NIH's decision to compare Genentech's Avastin and Lucentis for efficacy is excellent news since the price charged for them is markedly different ($280 vs $2000+). If they perform equally, as expected, savings for the public and Medicare could be enormous. Quite recently another VEGF binder, VEGF Trap was announced and is now in a large second phase study which, if it lives up to first phase results, promises another step in the quest to save vision.

And, while we tend to focus on vision loss, research has led to improved knowledge of PXE inheritance and cardiology care and treatment. The pace of change in scientific understanding and treatment of disease seems ever faster as is our ability to share discoveries around the globe.

PXE knows no borders. It is found worldwide in all racial, ethnic and cultural groups. NAPE's website draws contacts with PXE patients everywhere. As the year winds to a close, we look back to such contacts seeking information from India, Central and South America, Europe and the Middle East, as well as from Canada and around our nation. We respond to all without regard to geography or politics.

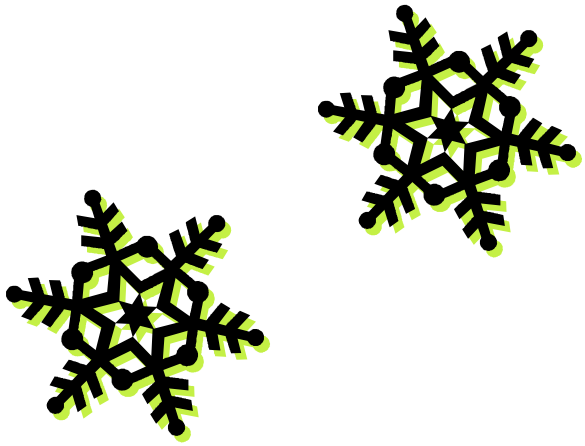
Lydia Chang and I are filled with hope, especially for younger PXE patients, and we rejoice in the communications revolution that makes contact so easy. In the season of joyful celebration by major faith groups, we dedicate this *PXE Awareness* issue to

hope. We celebrate recent advances in two major new research areas, stem cell and nanotechnology. Each offers new hope for the diagnosis and treatment of many disorders, including the major manifestations of PXE.

We begin this issue with one of our own coping with PXE-induced vision loss. Bill Guspie of Michigan shares strategies for using his remaining vision to lead a vigorous, involved life. We follow with a look at embryonic stem cell research related to vision. Finally Dr. Kattesh Katti, renowned for his breakthrough research in nanomedicine and nanotechnology, presents with his associate, Raghuraman Kannan, his response to my request for an explanation as to why PXE patients should be interested in this new research field. Both fields now are monitored closely by NAPE so that we can report to you as research efforts unfold.

In this joyous season we at NAPE wish for you a life brightened by peace, contentment and hope.

Fran Benham



Letter from Bill Guspie

Dear NAPE Friends,

While chatting with Fran Benham at the recent NAPE Conference in Detroit, I described my use of the Eccentric Viewing technique to make the best use of my remaining vision. I also mentioned that I still ride my bike and play golf. Fran asked me to share how I do these things for the newsletter. Here is my story.

I ride my bike using mostly the same routes, riding on the sidewalk as much as possible and wearing brightly colored clothes. So, along with my orange flag which is permanently attached to my bike, and wearing my helmet at all times, I am pretty well ready to go.

The picture shown is of me bringing home groceries from a store located less than a mile from where I live. The basket on the front of my bike holds one paper bag perfectly, and I make a couple of trips a week to the store. If I have a few extra items, I usually just carry them home in my backpack.

I also carry a cell phone and my white folding cane in the backpack, along with a note explaining that I am legally blind as well as an “If Anything Should Happen to Me” list including the names of people to contact, phone numbers and my insurance information. Using the backpack allows both of my hands to be free and to carry a few additional items without any strain. Using the bike is also great exercise!

When I go golfing, I bring a friend who stands behind me when I swing and tells me where the ball goes after I hit it. He is my “watcher.” This golf shot shows me putting and lining up a shot with the club facing the target line.

Another shot shows how I use the white cane to measure the distance from the ball to the hole.

A tip to other blind golfers: since normally amateurs will pick up the ball if the distance from the hole is within the leather grip on the putter, measure with the leather on your cane instead (it's longer...). Unfortunately, my very astute golfing buddies usually don't go along with this excellent tip – so when I'm with them, they show no mercy to the blind guy and I get NO SPECIAL ADVANTAGES!

Now on to Eccentric Viewing. One morning in the early 1990's, I woke up with some "fogginess" in one of my eyes. I thought I was just having a hard time getting focused after a hard night's sleep and, like many of you know, the condition kept getting worse. Several laser treatments later, most of the vision in the central point of my left eye was gone.

My doctor informed me it was essential for me to start using the Amsler Grid for both the right and left eyes because if my eye condition deteriorated, it would become more difficult for me to notice subtle changes in my vision. He asked me to note any waviness, blank spots, or changes within the grid lines of the Amsler Grid. I tested my vision at that time on a monthly basis. As my vision loss has now mostly stabilized, I only test with the grid about every 6 months.

One of the most important side benefits of using the grid is that it allows me to continually check for any vision changes that may occur. I'm then able to alert my doctor right away for possible treatment.

Following the loss of sight in my left eye, I learned that I have PXE. I began learning more about the disorder and how to manage daily tasks with what now is described as "low or limited vision." I came across a book that described a viewing technique known as "Eccentric Viewing" so I set about learning how to use it.

Here's what I do: In simple terms, this technique explains and gives suggestions on how to make use of the large portion of viewing area that remains after losing central vision. The viewing area of a person with normal vision is 180 degrees, left to right. Amazingly, it only takes approximately three degrees to the left and right of center to decrease our vision from 20/20 to more than 20/200, which is considered legally bind. That still leaves a whole lot of good

viewing area. The Eccentric Viewing technique shows you how to get to it in order to use it!

Using the Amsler Grid, I am able to detect the areas where I can still see objects and those areas where I cannot. It's important to test each eye individually to determine which one has the better vision. In my case, my right eye has the best vision, so I close or cover my left eye to perform the rest of the test.

I always start with a blank Amsler Grid and focus on the center dot. Then using a pen I rotate the grid clockwise from the outside of the grid border towards the center dot, while still focusing on the dot. Each time I lose sight of the point of the pen, I make a mark on the grid.

As I circle the grid, I think of it like the face of a clock. I typically make about three marks in each fifteen minute time interval, until I end up with about

twelve marks total when I reach high noon, the 12-o'clock position. The more marks you make, the better picture you will obtain of what you can and cannot see. I then connect the dots to make a shape.

The shape resulting from the test to my "good" right eye is irregular. The area inside the line is my blind area where I am unable to see anything. The area outside the line is where I still have viewing ability. Since the center dot of the Amsler Grid represents 20-20 vision, it is the area outside the line, but closest to the center dot, that is the area where one will have the best vision. The grid results showed that the area to the LEFT of the center dot on the Amsler Grid is where I have the greatest clarity to focus on an object.

Now is when the Eccentric Viewing technique comes into play. I point my nose at the object I'm trying to see, and lock my head and neck in that position. Here's the tricky part. I then move MY EYES ONLY and look to the RIGHT of the object that I am trying to see (the opposite of what the grid shows). Looking to the right actually moves my greatest clarity point (sweet spot) into position. If your sweet spot is to the right, you will actually look to the left of the object which, again, pulls that clarity point into position like a string pulls a toy train. It really works!

I now use the Amsler Grid not only to monitor changes in my vision, but also to verify that the areas where I focus the Eccentric Viewing technique are still the best areas (closest to the center dot on the Amsler Grid) to choose for viewing.

Using Eccentric Viewing has enabled me to do many of the same things I did before my vision difficulties, just more slowly, or with a bit of assistance. I am not able to do everything I used to do with full sight… but I refuse to become a hermit and have a daily pity party for myself! I will always be open to new ways and ideas to increase my remaining vision. I have to. After all, I'm now the proud GRANDPA of three very active grandsons (triplets), and I have to be able to convince them that I have eyes in the back of my head!

Happy Holidays,

Bill Guspie

PS: If you would like to contact me regarding this article, you may email me at billguspie@msn.com.

If you or another NAPE member have an interesting and positive way of coping with PXE problems, please let us know so that we can invite them to share their stories for the newsletter. Please contact the NAPE office with this information.

Amsler Grid

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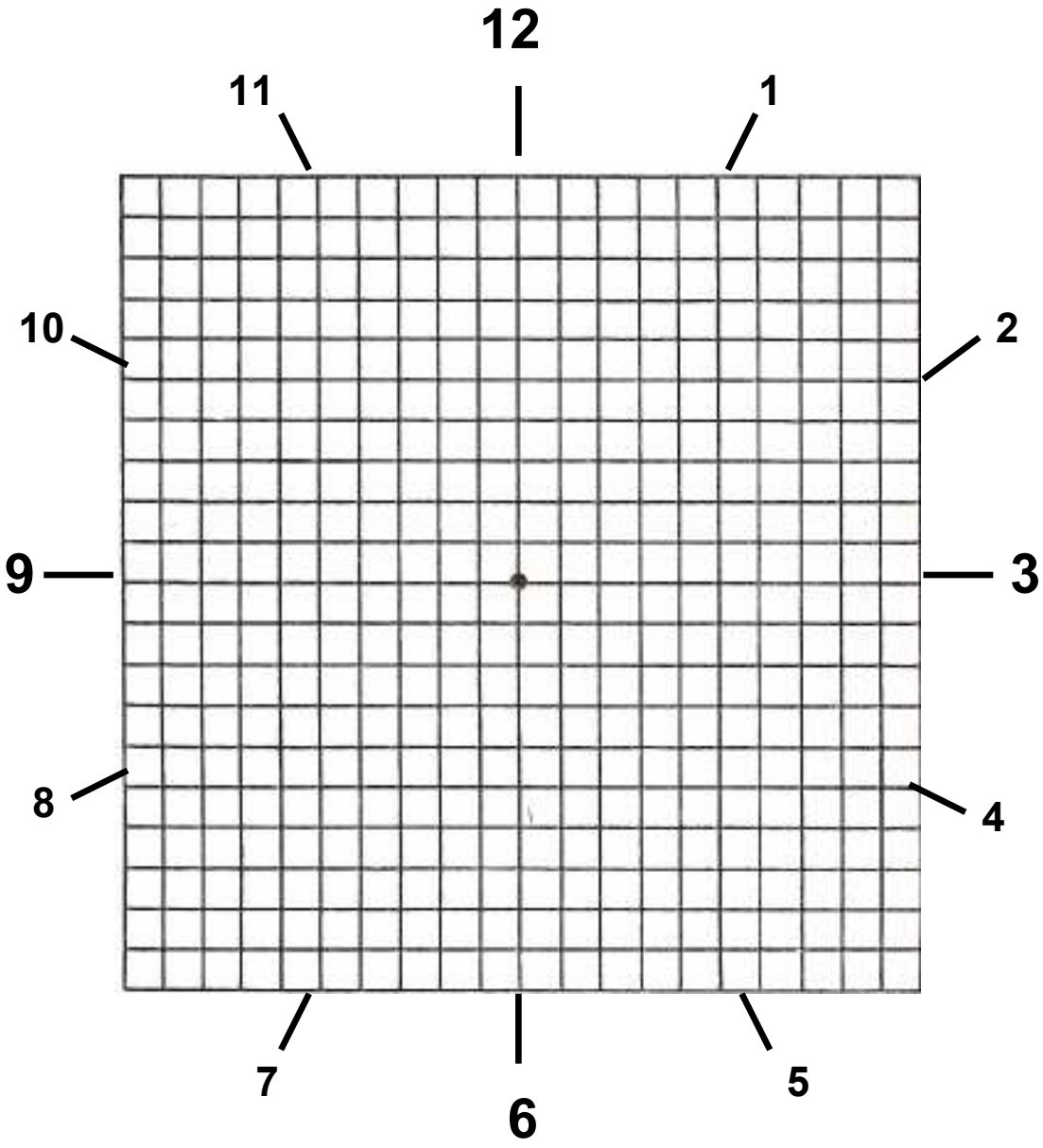

Embryonic Stem Cells and the Eye

By Frances Benham

The November midterm elections included stem cell initiatives in some states with the main focus on embryonic stem cell research. Vigorously contested by pro and con groups, the claims made created concern among voters. We at NAPE discussed the means intelligent voters might use to inform themselves outside the political arena. We follow research in a variety of venues routinely and were aware that one of the major claims against embryonic stem cell research was untrue – that no successful research has been done using embryonic stem cell lines. We decided to conduct a quick internet search, as we believe many of our readers do regularly, to see what, if any, evidence we might find in response to this oft-repeated claim.

We used the search engine Google with the search terms “regenerative medicine - retina” and “stem cell - macular degeneration.” Both searches yielded similar results. Since we know voters are interested in many disorders, we followed with similar searches using the topics “Parkinson’s Disease,” “diabetes,” “spinal cord injury” and “heart disease.” We learned that the scientific community worldwide is hard at work on studies using both embryonic and adult stem cells. This new field of study has captured commitment by many labs in universities, biotech companies and pharmaceutical companies.

So what did we find about embryonic stem cell research related to vision?

A highly important study identified had also received much popular media attention. “Human Embryonic Stem Cell-Derived Cells Rescue Visual Function in Dystrophic RCS Rats” by Raymond D. Lund, et al, is an eleven page scientific paper detailing the use of a number of embryonic stem cell lines differentiated into photoreceptor cells which injected into rats suffering from vision loss similar to AMD recovered vision. The study builds on previous research citing 31 studies, any of which can be found for further review. This complex study demonstrates that embryonic stem cell research has been successful, though the authors state that there is much work yet to be completed before treatments or cures can be available for visually impaired humans.

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The Washington Post carried a one-page item explaining the Lund, et al, study in lay terms. The *Milwaukee Journal Sentinel* published a longer article in lay terms about the Lund, et al, study and its exciting potential implications for overcoming human macular degeneration. *The New York Times* presented a similar report.

“Maternal Germ-line Transmission of Mutant mtDNAs from Embryonic Stem Cell-Derived Chimeric Mice” by James E. Sligh, et al, a six-page detailed scientific paper, describes a method using embryonic stem cells to introduce mutations in mice through the maternal germ-line. A variety of mutations were introduced, including those which result in visual impairment. Such mice are made available for research purposes to laboratories interested in studying disease processes and possible treatments or cures. Building on previous

research, the study cited 41 earlier studies which can also be reviewed. This successful study is important for the support it provides for other labs. It demonstrates that embryonic stem cell research is underway and has enjoyed success.

Science News Briefs reported the finding of human retinal stem cells capable of differentiating into all types of retina cells. The cells were isolated and implanted into newborn mice. Over a period of time these cells migrated and integrated into the test mice retinas. Written as a news item, the article carried only the name of the principal investigator, Derek Van der Kooy. It was the only study presented which was about adult, not embryonic, stem cell research relating to the eye found in our internet search which we believe represents internet searches by typical readers intent on informing themselves.

Nanomedicine: Should NAPE Be Interested?

By Kattesh V. Katti and Raghuraman Kannan,
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Introduction

Nanotechnology is projected to be a major key to 21st century technological and medical progress, and its success will depend on continued collaborative innovative efforts among the natural sciences, medicine, engineering and allied disciplines. Although it may be too early to gauge, its economic and societal impact is estimated by the National Science Foundation report “Societal Implications of Nanoscience and Nanotechnology” (March 2001) at one trillion dollars by 2015 [1]. This new field, referred to as “Disruptive Science,” is inherently interdisciplinary and has the power to break boundaries between traditional areas of science, agriculture, medicine and engineering. It opens new opportunities to miniaturize today’s products, to provide new materials with exceptional performance properties and to enrich our understanding of nature and life itself. This interdisciplinary field is being discussed in terms of its potential to deliver a Second Industrial Revolution, radically transforming manufacturing processes. In medicine it is poised to

bring about a paradigm shift in the way diseases are diagnosed and treated.

Nanomedicine is an emerging medical area that utilizes nanoparticles for the detection and treatment of various diseases and disorders. It relies on nanoparticles which are tiny fragments of metals (or non-metals) that are 100,000 times smaller than the width of human hair. Why is this tiny size so important in medical applications? Size is important; but, it is not size alone that matters. It also is the collateral properties that emanate when materials, especially metals, are reduced to nanometers. As shown in **Figure 1**, nanoparticles within the size domains of 1-50 nanometers can be related to the sizes of various biological entities including cells, viruses, proteins and antibodies.

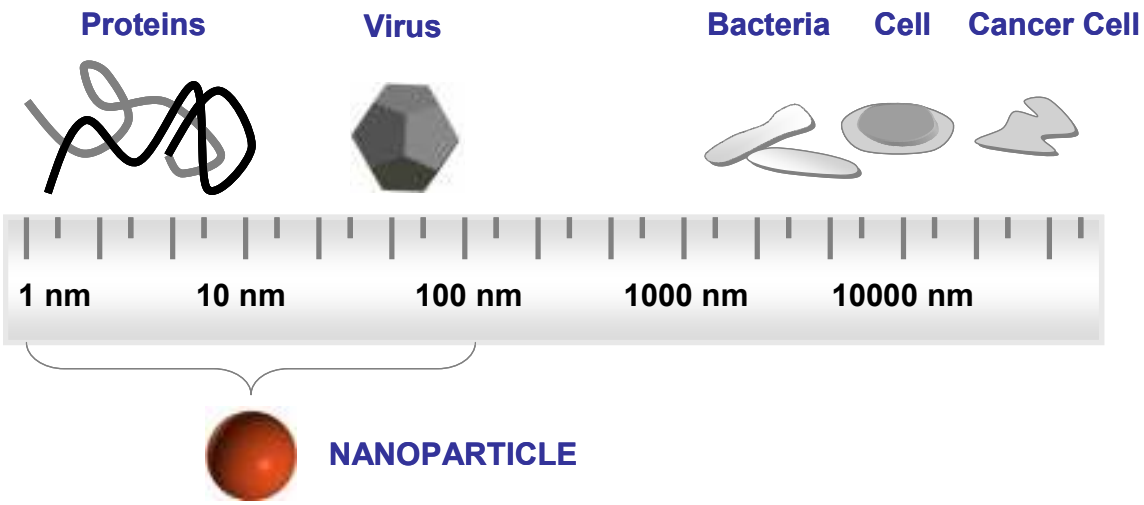

Figure 1: Size Inter Relationships of Nanoparticles with Cells, Viruses and Other Biologically Relevant Species

Man-made nanoparticles, with sizes in the range of living cells, are the focus of current medical research. Nanoparticles produced using nanoscience and nanotechnology principles exhibit properties unique to nanometer size. For example: (i) gold nanoparticles can release a certain amount of heat when placed within oscillating magnetic fields for potential applications to control or eradicate specific tumors; (ii) nanoparticles display photo absorbance or emission characteristics that can be used in imaging for the diagnosis of various diseases; (iii) selective absorption of x-rays by metallic nanoparticles can lead to measurable contrasts for use in computer tomographic (CT) imaging of diseases/disorders. Release of absorbed x-ray energy onto tumors can suppress or eradicate them, thus utilizing nanoparticles as mediators for dual imaging and therapy applications to diagnose, stage and treat various diseases. These and a host of useful diagnostic/therapeutic properties are attainable only when metallic (or non-metallic) substances are reduced to nanometer sizes, thus making the interplay of size and properties of nanoparticles the essence of an emerging medical modality referred to as nanomedicine (**Figure 2**) [2].

A variety of such nanoparticulate vectors and nanoscale devices have demonstrated efficacy in their utility as *in vivo* tumor imaging agents in animal models and in human clinical trials. The ubiquitous place of gold in nanomedicine stems from its chemical ability to serve in an unoxidized state at the nano size when most surfaces of less noble metals oxidize to a

depth of several nanometers or more, often obliterating their nanoscale properties. The high reactivity of gold nanoparticles (AuNPs) juxtaposed with their biocompatibility has spawned great interest in their utility for *in vivo* imaging and therapy. Recent work is centered around development of hybrid AuNPs starting from nascent metal nanoparticles. Hybrid nanoparticles are produced by coating AuNPs with tumor cell specific biomolecules, including monoclonal antibodies, aptamers, peptides and various receptor specific substrates. Receptor specific hybrid nanoparticles are used mainly for targeting three different markers that are over-expressed on cancer cells. They include: matrix metalloproteases (MMPs), epidermal growth factor receptor (EGFR), and oncoproteins that are associated with human papillomavirus (HPV) infection.

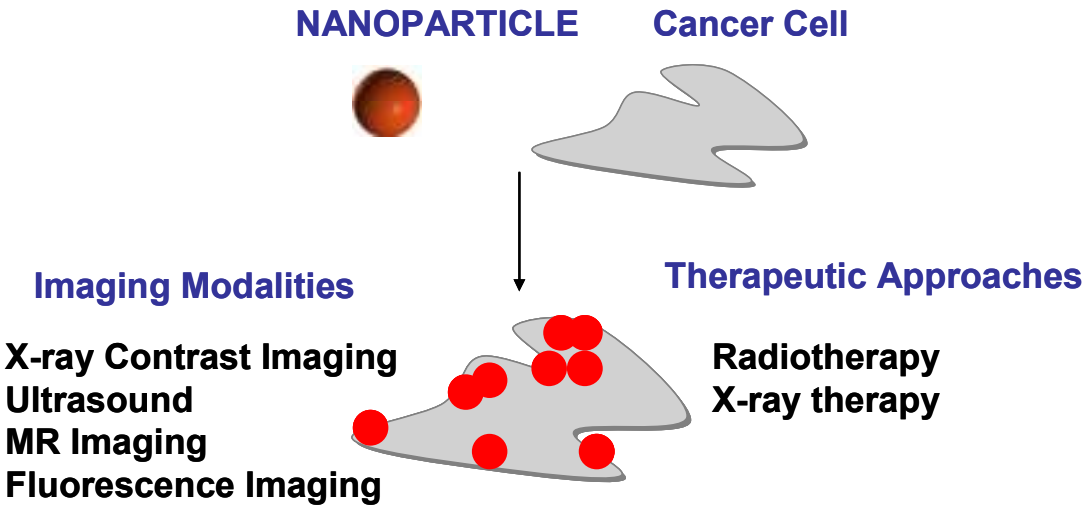

Figure 2: Targeted Delivery of Nanoparticles to Cancer cells for Diagnosis and Therapy

Synthesis of Biocompatible Gold Nanoparticles

Biocompatibility is an important prerequisite in utilizing AuNPs for *in vivo* imaging and therapy applications. It requires the stabilizing of nanoparticles in a biologically benign medium. Currently available techniques utilize harsh conditions, such as the application of sodium borohydride to reduce $AuCl_4^-$ in order to produce AuNPs. While these methods work efficiently, they are unsuitable because sodium borohydride will reduce the chemical functionality present on peptide backbones, either reducing or eliminating the biospecificity of the biomolecules. The sodium borohydride reduction method also uses thiols to stabilize AuNPs from agglomeration. Although this protocol leads to enhanced stability of AuNPs, such AuNPs cannot be readily anchored onto peptides or other biomolecules because of the strong interaction of gold metal with thiol groups. This means that thiol-stabilized AuNPs have limited applicability in the development of AuNP tagged biomolecules for use in target-specific nanoscale imaging or therapeutic agents. Other methods described in the literature have similar drawbacks.

For sustained research aimed at the design and development of AuNP-based imaging or therapeutic agents, we felt it imperative to develop new and efficient methods that lead to the production of biocompatible AuNPs under physiologically benign conditions, using biologically benign chemical molecules such as carbohydrates (starch, glucose,

agarose) and proteins (e.g., glyco proteins). As part of our long standing interest in the design and development of gold and other metal-based cancer imaging and therapeutic agents and sensor devices [3-10], we performed extensive studies on the chemical, structural, photophysical and biological aspects of a wide spectrum of gold compounds. We recently discovered that a new trimeric alanine phosphine conjugate (THPAL, $P(CH_2NHCH_3COOH)_3$), interacting with commercially available $NaAuCl_4$ in water at 25 ^{0}C at physiological pH, results in the production of biocompatible gold nanoparticles in excellent yields with complete retention of nanoparticulate properties [3,4]. This AuNP production process allows systematic variation in nanoparticulate size via changes in the stabilizer and stoichiometry of $NaAuCl_4$ and THPAL (**Figure 3)**.

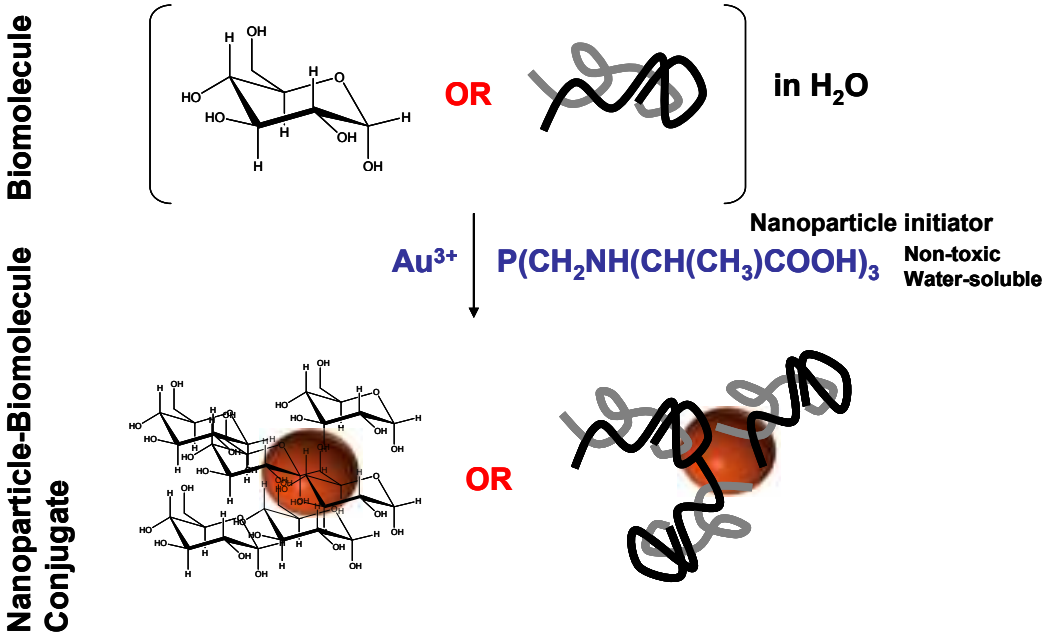

Figure 3: New processes for the Production of Biocompatible Gold Nanoparticles

Extensive studies of the interrelationship of reaction conditions and nanoparticulate sizes have provided optimized conditions to produce AuNPs of well-defined sizes. Transmission electron microscopic (TEM) analysis has been used to view gold nanoparticulate sizes that are 100,000 times smaller than the width of human hair. Sizes and shapes of gold nanoparticles are depicted in **Figure 4**. We have used various biocompatible matrices including, starch, agarose, glucose, and Gum Arabic to stabilize gold nanoparticles. The sizes of resulting AuNPs are: Starch stabilized: 20 nm, Agarose stabilized: 13 nm, Glucose stabilized: 22 nm, and Gum Arabic stabilized: 10 nm. These nanoparticle size variations are ideally suited for biomedical applications because 15-30 nm sizes allows direct attachment of gold nanoparticles to specific cells for diagnostic imaging and therapy applications.

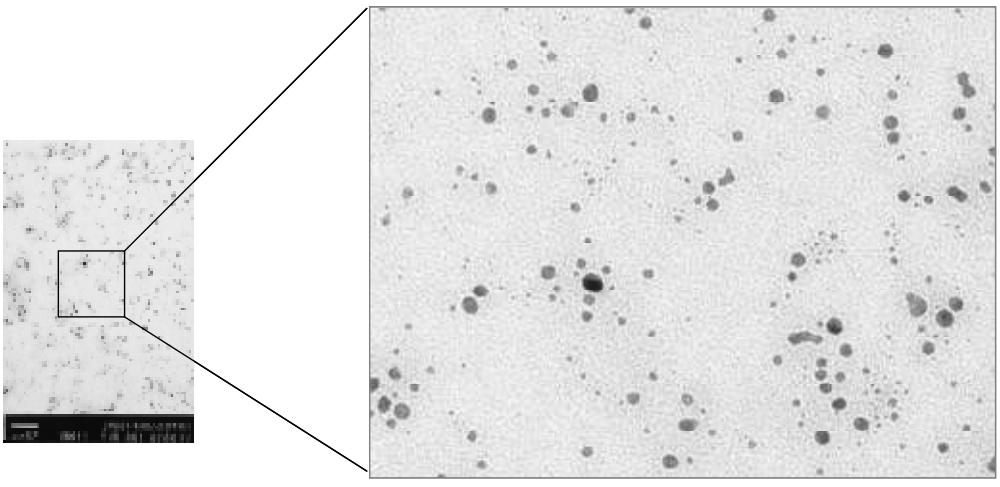

Figure 4: Transmission Electronic Microscopic Pictures of Nanoparticles that are 100,000 times smaller than the width of Human Hair

Detection and Therapy of Early Stage Diseases

Nanoparticles, because of their sizes within the cellular domain, can be effectively used to target individual cells for early stage detection and therapy of cancer and other diseases. Almost all types of mammalian cancers over-express receptors for specific peptides (and proteins). Therefore, cancer specific peptides can be anchored on the surface of nanoparticles to give them the “sense of direction” to seek and home in selectively onto tumor cells and cancer tissue. Because of the large surface area of nanoparticles, each one can carry more than one peptide or more than one type of peptide (**Figure 5**). This multifunctionality not only leads to significantly higher diagnostic/therapeutic efficacy, the incorporation of peptides with multiple receptor targeting capabilities produces multiple antigen-binding nanoparticles for targeting multiple cancer receptors in patients. Schematic sketches, as shown in **Figure 6**, outline new approaches being developed in our laboratory for the creation of prostate tumor-specific hybrid gold nanoparticles for use in imaging and therapy.

Impairment of vision is a common manifestation in various ophthalmic diseases and disorders, including age related macular degeneration and pseudoxanthoma elasticum. Potential treatment approaches based on gold nanoparticles are on the horizon for these problems thanks to the biocompatibility of gold nanoparticles and their ability

to deliver diagnostic/therapeutic probes without harmful side effects.

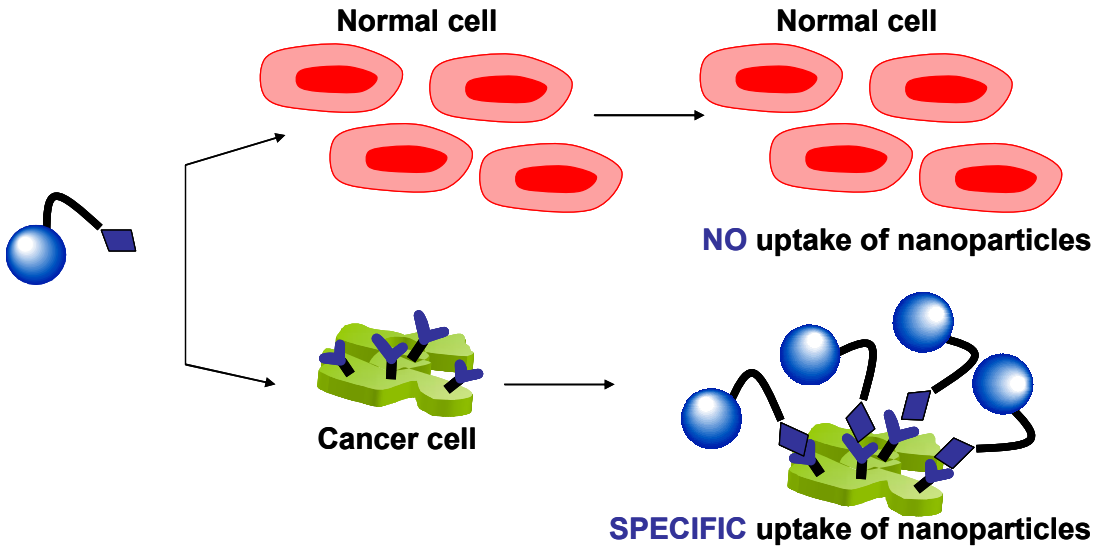

Figure 5: Giving a 'Sense of Direction' to Gold Nanoparticles: Conjugation of Gold Nanoparticles with Cancer Specific Peptides

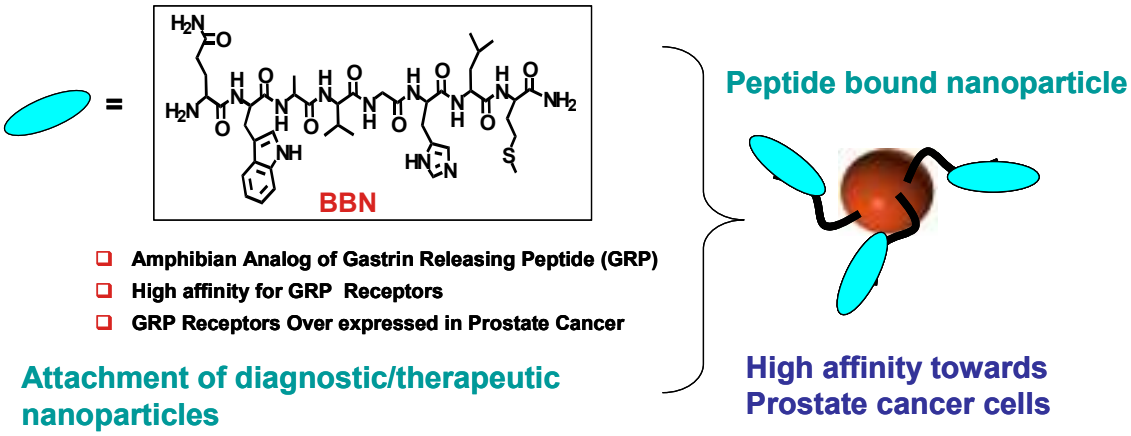

Figure 6: New Approaches for the development of Prostate Tumor Specific Gold Nanoparticles for Imaging and Therapy of Prostate Cancer

Gold Nanoparticles In Therapy

Another attractive approach for the application of nanotechnology to nanomedicine is the utility of nanoparticles that display inherent therapeutic properties. For example, radioactive AuNPs present attractive prospects in cancer therapy and other diseases. The radioactive properties of Au-198 (βmax = 0.96, MeV; t½= 2.7 d) and Au-199 (βmax = 0.46 MeV; t½= 3.14 d) make them ideal candidates for use in radiotherapeutic applications. Such gold isotopes have imageable gamma emissions for dosimetry and pharmacokinetic studies. Gold nanoparticles can be delivered directly into cells and cellular components with a high concentration (dose) of radioactivity to cancerous tumor cells. Nanoparticulate therapeutic agents derived from radioactive AuNPs provide higher therapeutic payload to tumor sites as each gold nanoparticle contains hundreds/thousands of atoms of gold. This unique advantage of achieving a substantial increase in therapeutic dose to tumor site coupled with the feasibility of tagging nanoparticles of Au-198 with oligonucleotides and peptides that are selective for receptors over-expressed by diseased tissue, presents a remarkable new potential for the treatment of cancer. Recent studies in our laboratories have provided “Proof of Principle” for the production and stabilization of biocompatible radioactive gold nanoparticles for potential applications in therapeutic nanomedicine (**Figure 7**) [3].

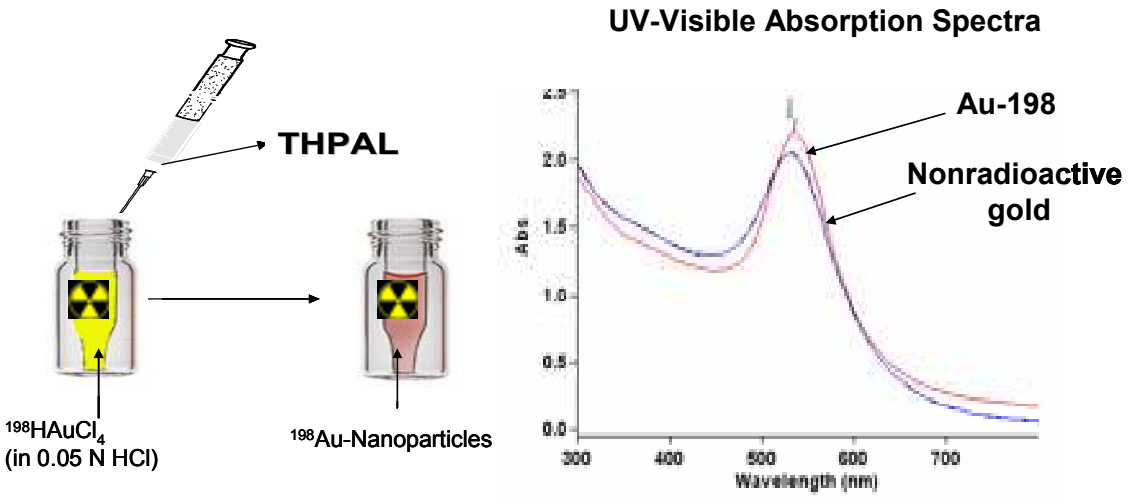

Figure 7: New Approaches for the production of Therapeutic Nanoparticles

Readily Injectable Nontoxic Gold Nanoparticles for Treating Cancer and Other Disorders

Cancer and other disorders often require repeated administration of medication, making the development of nontoxic pharmaceuticals of major significance in modern treatment protocols. From the above discussions, it is clear that gold nanoparticulate vectors can play a significant role in the advancement of clinically useful diagnostic and therapeutic medical products. A serious drawback in this effort is the rarity of nontoxic gold nanoparticulate constructs and formulations that can be administered as described. The ability of plants to absorb and assimilate metals provides the potential to utilize plant extracts as nontoxic vehicles to stabilize and deliver nanoparticles for *in vivo* nanomedicinal applications. In this context, we have recently discovered the application of Gum Arabic (Acasia Gum) as a plant-

derived construct for stabilizing gold nanoparticles. This natural gum is exuded by various species of Acacia commonly grown in the sub-Saharan regions of Africa, Australia, India and South America. Gum Arabic is a widely accepted nontoxic ingredient in both food and pharmaceutical products. Emulsification, acid stability, low viscosity at high temperatures, adhesive and binding properties and good mouth feel are among the reasons for its wide acceptance as an additive in confectionaries, beverages, bakery products, brewing, and in pharmaceutical formulations. In addition, Gum Arabic has unique structural features that attracted our attention. It has a highly branched polysaccharide structure consisting of a complex mixture of potassium, calcium and magnesium salts derived from arabic acid with galactose, rhamose, glucuronic acid, 4-O-methyl glucuronic acid and arabinos residues. Its molecular structure is comprised of three main components: the dominant being arabinogalactan (90%) which has a low protein content (5%), a high protein content (10%) segment with 10% arabinogalactan and the third component (<1%) contains glycoproteins with over 50% protein content. Our recent studies have produced a new class of injectable, *in vivo* stable hybrid nanoparticles derived from the tagging of Gum Arabic glycoprotein matrix with gold nanoparticles (**Figure 8**). Preliminary results of *in vivo* pharmacokinetics studies of GA-AuNP in pigs have demonstrated that these nanoparticulate phyto-constructs are nontoxic and thus may be utilized for human imaging and therapy applications [4].

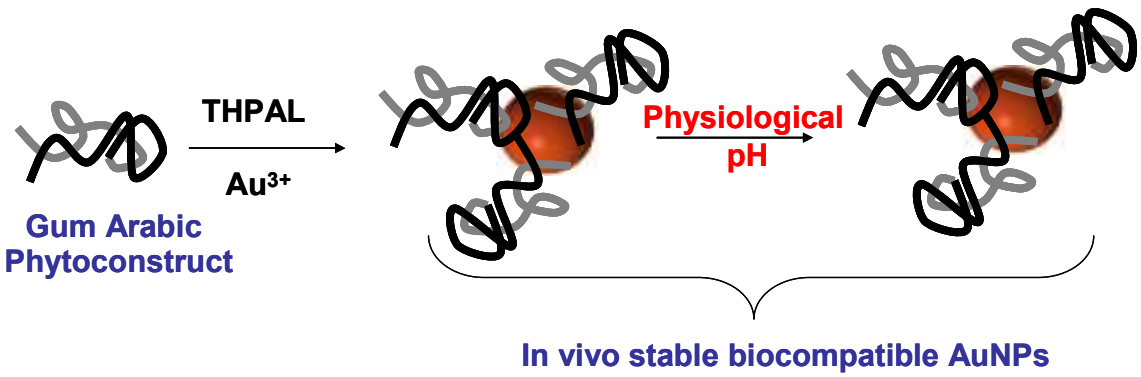

Figure 8: Production of Readily Injectable Non Toxic Gold Nanoparticles Derived from Gum Arabic Phyto Stabilizers

Societal Impact and "The Big Nanomedicine Picture"

The unique abilities of nanoparticles to serve as diagnostic/therapeutic probes and also as carriers of drug molecules for delivery at specific sites provide exciting opportunities in treating various diseases. Nanoparticles present realistic prospects to serve as platforms for carrying both diagnostic and therapeutic vectors within the same entity, and thus may provide future pharmaceuticals with both capabilities built within the same pill. Indeed, it has been estimated that over 80% of all future drugs will utilize some form of nanotechnology. "Readily Injectable" gold nanoparticles that are stable *in vivo* and nontoxic at therapeutic doses will play pivotal roles for site-specific *in vivo* delivery, as *in vivo* sensors, semiconducting slow bleaching photo-active agents for optical imaging, as carriers of very high diagnostic or therapeutic loads to tumor/disease sites, in photodynamic therapy by carrying a plethora of free

radical-generating chemicals to tumor sites, as contrast enhancers in CT imaging and as x-ray absorbers at tumor sites for x-ray based therapy. Conjugation of nontoxic gold nanoparticulate vectors to stem cells will provide major advances in stem cell based imaging and therapy of cancer and other disorders. Despite the “super spectrum” of current and realistic future applications offered by hybrid gold nanoparticles, there is still a severe paucity of *in vivo* studies demonstrating low toxicity of gold nanoparticulate constructs and formulations. Therefore, the development of readily injectable, *in vivo* stable nontoxic gold nanoparticulate vectors, especially created from commonly accepted human food ingredients, are needed for major advances in nanomedicine. Our results demonstrating the ability of Gum Arabic to provide *in vitro* and *in vivo* stability to maintain the nanoparticulate properties of gold nanoparticles intact for several months in aqueous/saline/phosphate buffered solutions, as well as in the solid state, represent a significant advance in nanoscience with realistic implications for safe delivery of nanoparticles for a variety of diagnostic and therapeutic applications. The ready availability and adaptability of Gum Arabic within the human food chain make our approach a viable strategy for storage, shipment and *in vivo* delivery of gold nanoparticle-based nanomedicine products world wide.

Although there is no question of the scientific power and the positive impact of nanoscience and nanotechnology in transforming medical diagnosis

and therapy, the potential toxic side effects of nanoparticles administered via intravenous or oral pathways cannot be discounted. Concerted effort must be invested in gaining new insights concerning near and long term pharmacology and toxicology of a wide spectrum of nanoparticles that are being considered for medical use.

Acknowledgment: This work has been generously supported by the National Institutes of Health/National Cancer Institute under the Cancer Nanotechnology Platform program (grant number: 1R01CA119412-01).

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