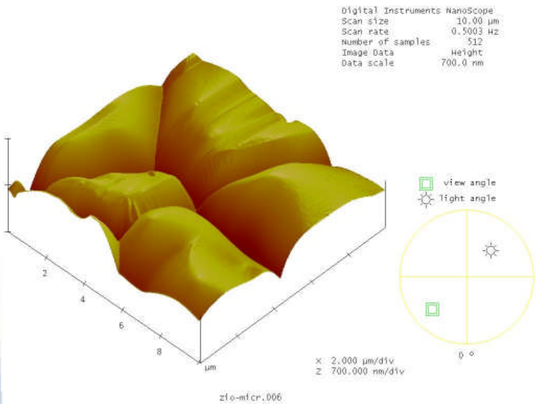
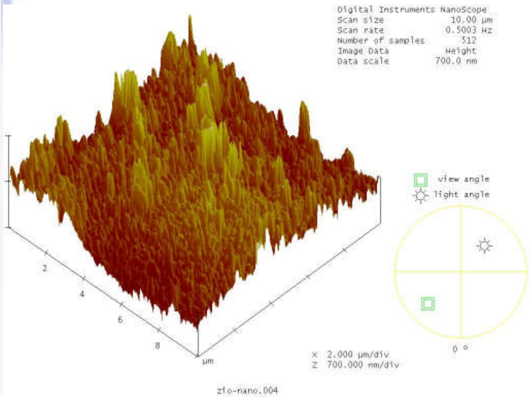
Nanospherical Ceramics: Resisting Bacteria Infection

While increasing bone cell functions, nanomaterials reduce bacteria functions.

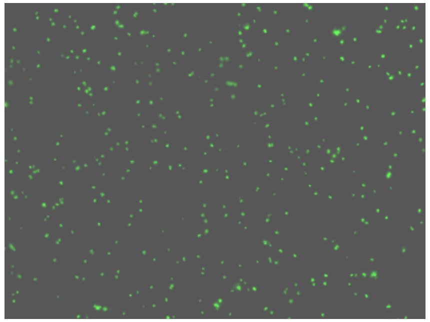


Conventional ZnO

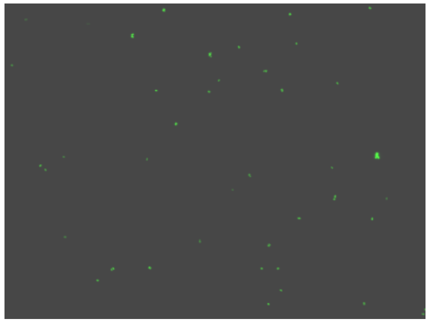


Nanophase ZnO

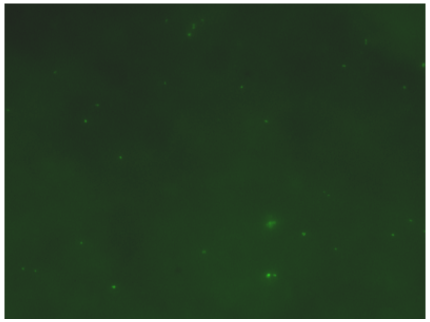
S. Epidermis



Positive Control (Wrought Ti)



Conventional ZnO

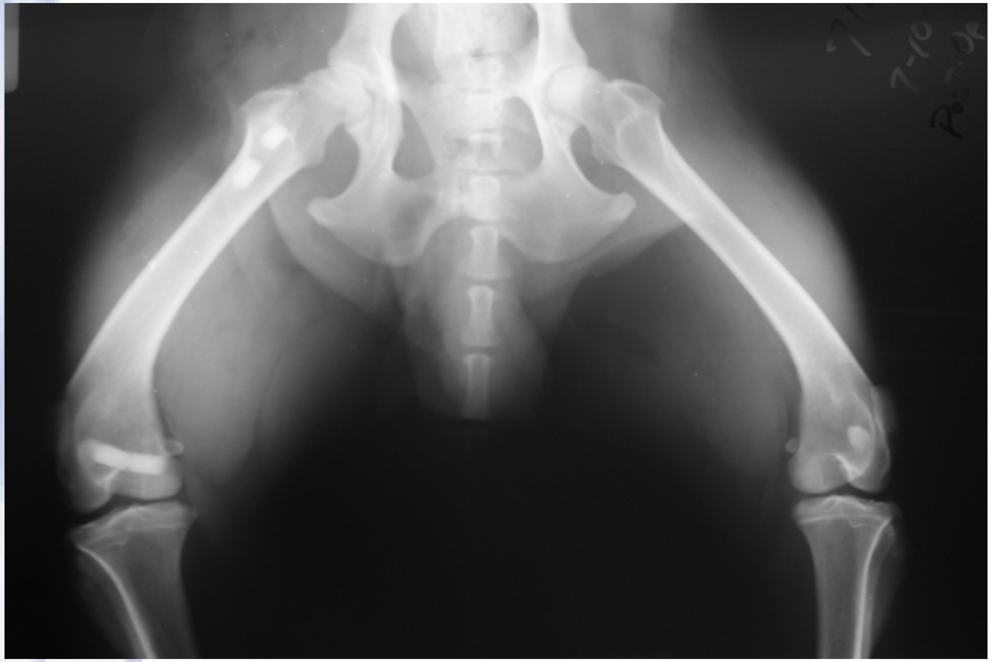


Nanophase ZnO

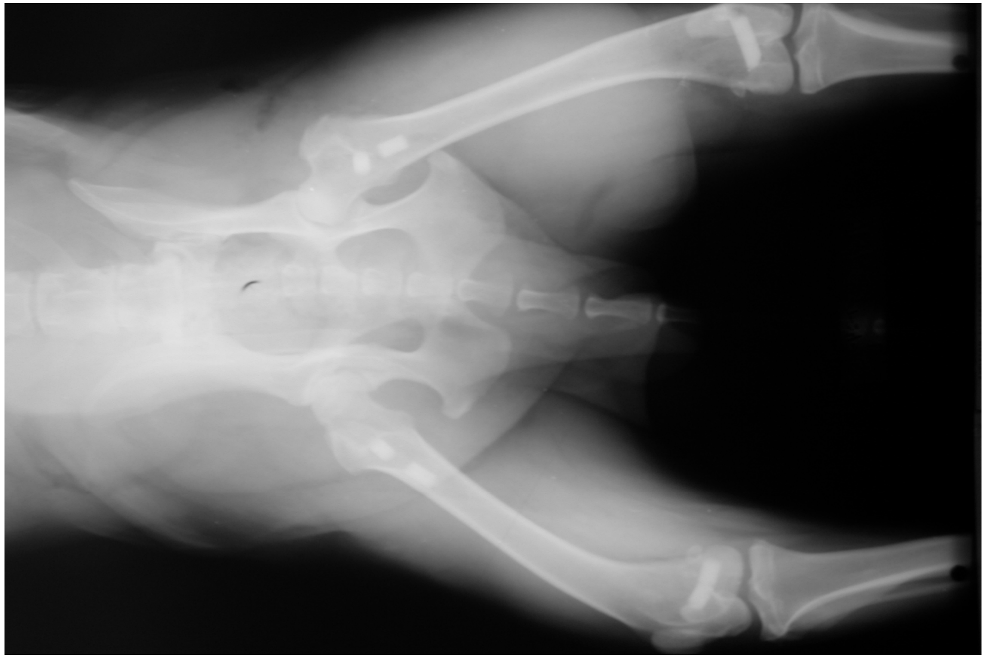
Mag. = 400X

Angstrom Medica:
Bilateral Canine Osseointegration
Distal and Proximal Femur

2 weeks



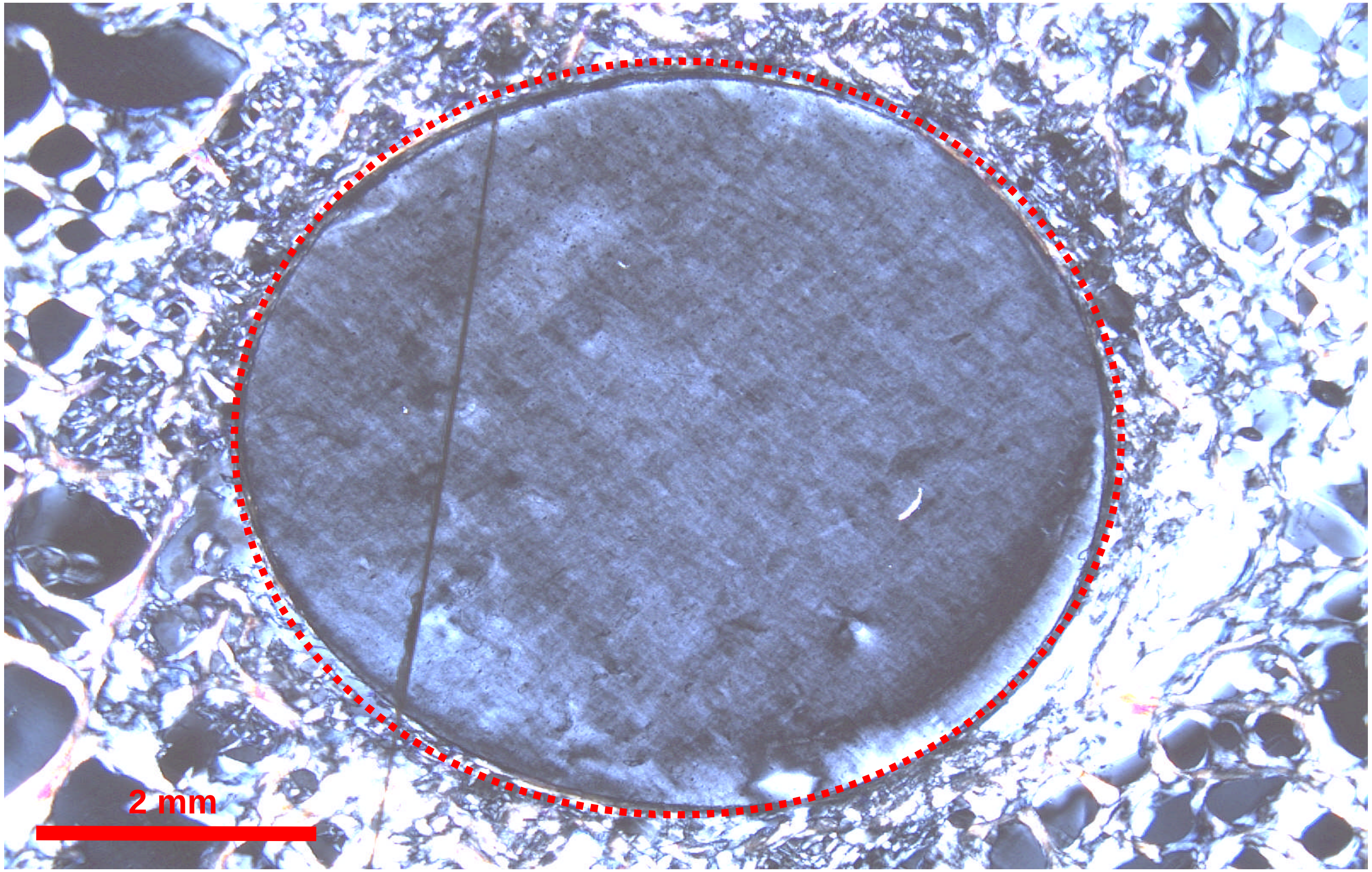
4 weeks



Bone Bonding		
	NanOss™ HA	2 weeks
	Conventional HA	8 -12 weeks
	Titanium	10-14 weeks
	Stainless Steel	12-16 weeks
	Polymers	Does not bond

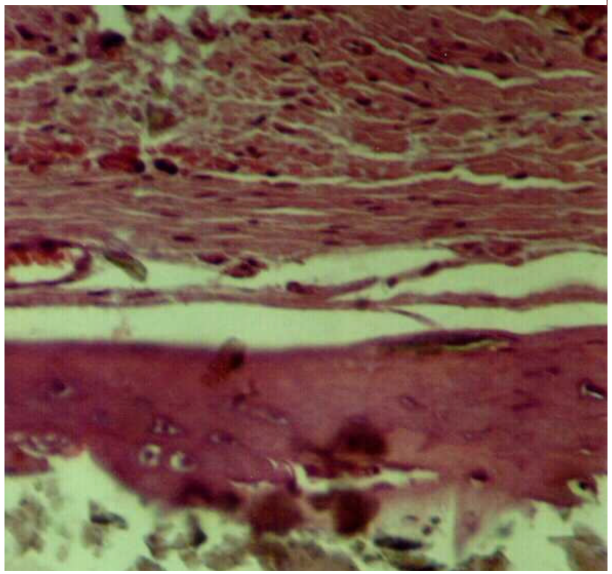
Angstrom Medica

Osseointegration at 4 weeks

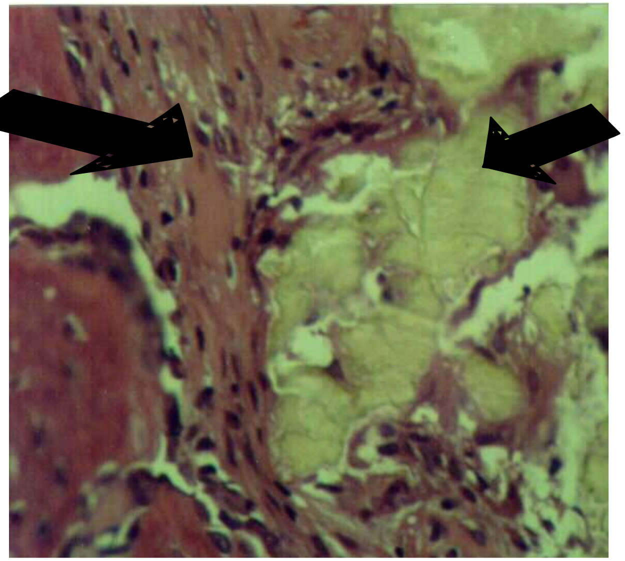


Distal Femur

Histology Sections of Nanophase Alumina Implanted Into Neonatal Rat Calvaria



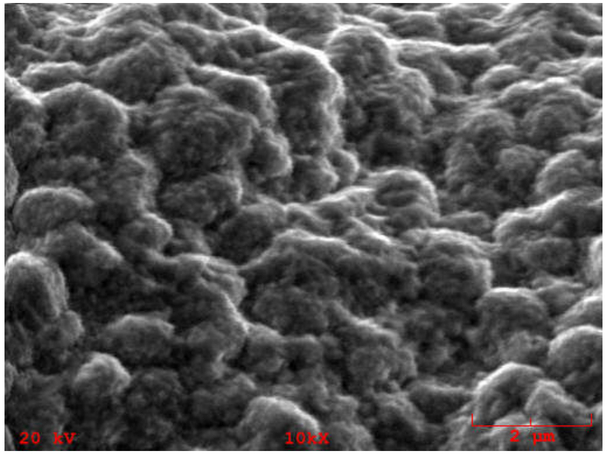
24 nm (nanophase) grain size alumina



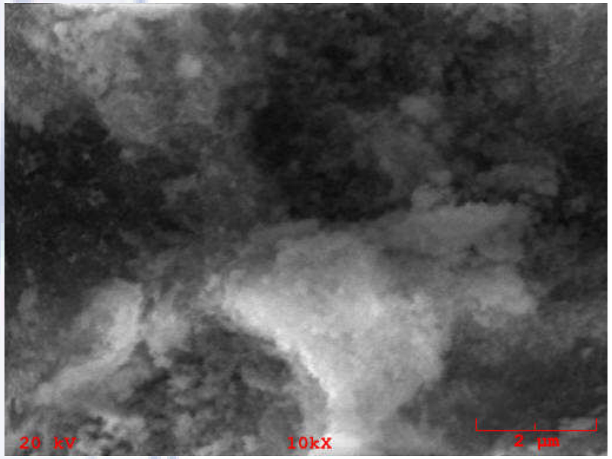
177 nm (conventional) grain size alumina with PLGA

Implantation time: 8 weeks. Stain: H & E.

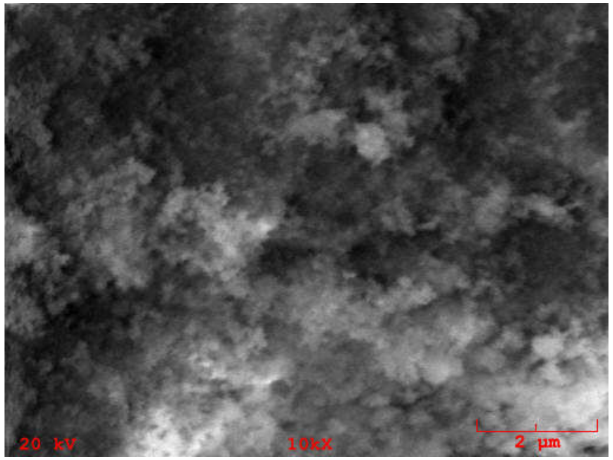
COATINGS
Nanospherical Ceramics



Uncoated Ta Scaffolds

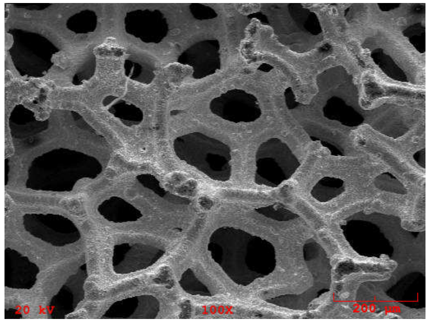


Conventional HA Coated Ta



Nano HA Coated Ta

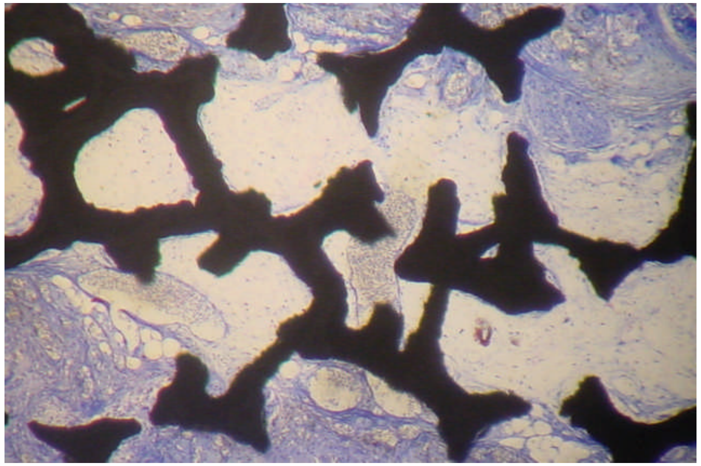
Working in collaboration with Spire Biomedical, using their IonTite™ technology, we have coated traditional orthopedic implant materials with nanospherical ceramics to increase bone growth.



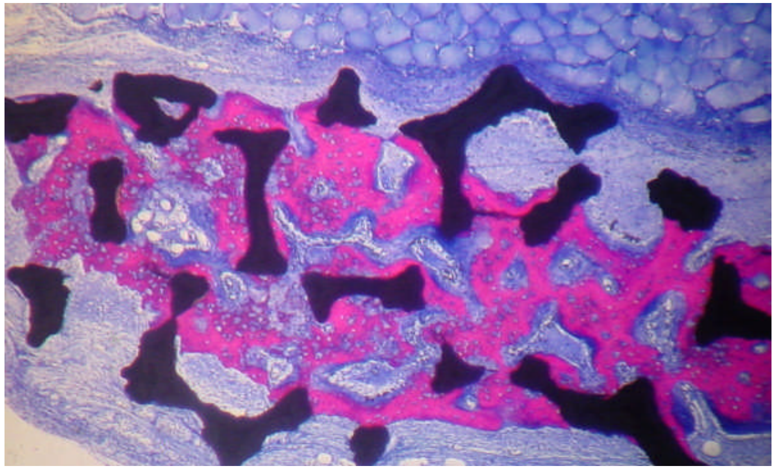
Ta Scaffold

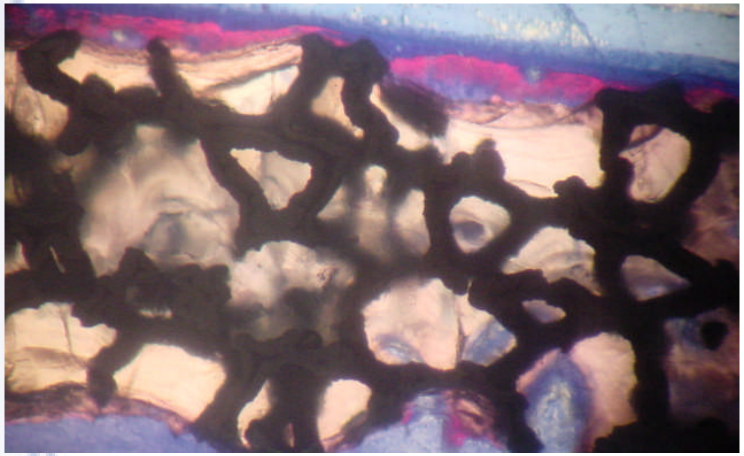
COATINGS
Nanospherical Ceramics

Implantation Time = 2 weeks; Animal Model = rat calvaria

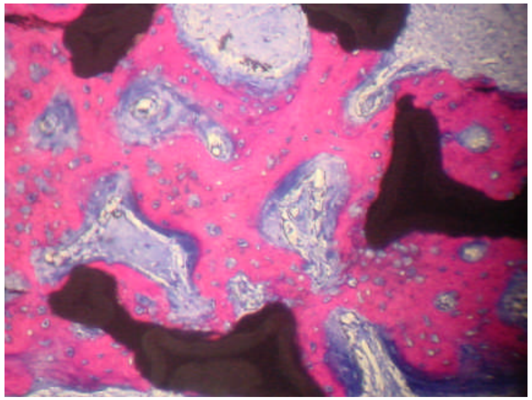


Uncoated Ta Scaffolds





Conventional HA Coated Ta



Nano HA Coated Ta

PART I (cont.)

BONE: Nano-fiber Ceramics

Ferromagnetism above Room Temperature Discovered in Mn-Doped ZnO

Ferromagnetism at and above room temperature in magnetic semiconductors is a property of significant interest for spintronic applications and devices. Mn-doped ZnO and GaN have been predicted, based on theoretical calculations, to be potential candidates for exhibiting ferromagnetism above room temperature, leading to an intense search for the right material. The first observations of ferromagnetism above room temperature for dilute Mn-doped ZnO have now been reported. K.V. Rao, P. Sharma, and their colleagues from the Royal Institute of Technology (Sweden) and from the Armament Research Center (United States), Arizona State University (United States), University of Uppsala (Sweden), and the University of Sheffield (United Kingdom) report this discovery in both bulk and thin transparent films of Mn-doped ZnO in the October issue of *Nature Materials*.

The incorporation of ferromagnetism in ZnO, a known piezoelectric and electro-optic material, may lead to various multifunctional properties. Doping ZnO with Mn, a 3*d* transition metal, can make possible the injection of a large amount of spins and carriers, making Mn-doped ZnO an excellent candidate for spintronic applications.

In this study, the material was made by mixing appropriate amounts of ZnO and MnO_2 powders. The powder mixture was then calcined at 400°C for 8 h and then sintered at temperatures ranging from 500°C to 900°C for 12 h to obtain $Zn_{1-x}Mn_xO$ (x = 0.01, 0.02, and 0.1). For samples sintered below 700°C, superconducting quantum interference device measurements revealed ferromagnetic ordering. Elemental mapping using electron dispersive spectroscopy showed that the Mn was uniformly distributed and the material was homogeneous with a single phase. Sintering the samples above 700°C suppressed the ferromagnetism to below room temperature. This was attributed to the formation of Mn clusters, which are antiferromagnetic, and/or the formation of other phases. Ferromagnetic resonance (FMR) measurements indicated that the 2 at.% Mn-doped ZnO is a ferromagnetic semiconductor with a Curie temperature T_c well above 425 K. The researchers said that this is likely the first FMR measurement of room-temperature ferromagnetism in a semiconductor.

Thin films of the $Zn_{1-x}Mn_xO$ were deposited on fused quartz substrates using a pulsed laser ablation technique. The films, which were transparent, also exhibited room-temperature ferromagnetism and phase homogeneity. High-resolution transmission electron microscopy on the thin films showed that the ZnO was ordered and oriented perpendicular to the *a–b* plane of a hexagonal lattice with a matching lattice parameter. The results suggest that the Mn substitutes for the Zn in the structure. This discovery of above-room-temperature ferromagnetism in Mn-doped ZnO semiconductors opens up a number of possibilities for spintronic applications and novel magneto-optical components.

GOPAL RAO

Large Diamond Crystals Grown at Low Temperatures

Synthetically made diamond is widely used for technological applications ranging from abrasives, tool coating, microelectronics, and optics to corrosion protection. Yet most techniques for making this material require high temperatures and pressures. Qianwang Chen, a professor of materials science and engineering at the University of Science and Technology of China, and his colleagues have made diamond crystals as large as 510 μm in size by reducing magnesium carbonate with sodium at temperatures as low as 500°C.

As reported in the September 29 issue of *Angewandte Chemie*, the researchers were able to carry out the reaction in an autoclave using autogenetic pressure. The preferential formation of diamond over graphite was found to be very sensitive to conditions of temperature, pressure, and starting concentration of reactants. The researchers think that magnesium carbonate is first pyrolyzed to yield the oxide and supercritical carbon dioxide. The latter is then reduced on the surfaces of molten sodium at high pressures to give the polyhedral diamond crystals, which are usually about 120 μm in length and can be as large as 510 μm. At 500°C and 860 atm pressure, reaction yields of up to 6.6% were attained. Raman spectroscopy and x-ray diffraction showed the formation of high-purity, well-crystallized diamond particles. Moreover, the researchers said, the diamond crystals are transparent and colorless. No diamond could be detected at process temperatures below 500°C.

Chen said, "It was in 1796 that it was shown that diamonds could be stoichiometrically converted to carbon dioxide by burning in oxygen, only now has it been possible to achieve the reverse conversion of dense carbon dioxide to large diamond crystals."

While the mechanism for carbonate reduction and diamond growth is not fully understood, the low cost of the starting materials and low temperatures used in this process make this technique particularly attractive for industrial diamond production.

SARBAJIT BANERJEE

Arrays of Binary and Ternary Particles Fabricated by Use of Patterned Microchannels

Patterned arrays of nano- and micron-sized particles have great potential as materials for high-performance electronic and optical devices. In the November 4 issue of *Chemistry of Materials*, researchers Seung-Man Yang and co-workers from the Korea Advanced Institute of Science and Technology report a method for fabricating binary and ternary particle arrays using patterned microchannels. This method began with a poly(dimethylsiloxane) mold containing V-shaped grooves of precise dimensions. These grooves were filled with silica spheres 320 nm or 600 nm in diameter or with polystyrene (PS) spheres 1.01 μm in diameter using a dip-coating technique. The spheres are driven into close-packed arrays in the V-shaped grooves by capillary forces. The confined geometry of the grooves also directs the spheres into a fcc structure with the (100) plane toward the facing surface. After these V-shaped arrays of particles are transferred to a polyurethane film, the resulting new grooves can be filled with spheres of other types and diameters to produce binary particle arrays. For example, 1.01 μm diameter PS spheres could be placed into the grooves between V-shaped arrays of the 320 nm or 600 nm silica spheres. Alternatively, filling those grooves with a mixture of 50 nm diameter silica spheres and 1.01 μm diameter polystyrene spheres leads to a ternary particle array. Subsequent oxygen plasma etching selectively removes the polystyrene particles, leaving patterned, inverted-pore structures in the material. The researchers indicated the potential for using this technique for the fabrication of "display devices, 2D photonic crystals, and ordered open-pores structures" that could be used as "templates for nonspherical aggregates of colloidal particles."

LARKEN E. EULISS

Nanofiber Alumina Enhances Osteoblast Function for Orthopedic Implants

Some key questions in biomaterials address the bonding of bone to implant surfaces for dental and orthopedic applications. In their study on osteoblast function on anisotropic nanoparticulate compounds, researchers from Purdue Univer-

sity and Argonide Corporation (Sanford, Fla.), led by Thomas J. Webster of the Department of Biomedical Engineering a[t] Purdue, found that osteoblast function and consequently bone formation on the implant depend strongly on the topology of the implant's surface and the morpholo[-]gy of crystallites. They said that the shape and size of the nanophase implant parti[-]cles are consistent with the dimensions o[f] hydroxyapatite particles of natural bone. In general, the researchers identify three factors that promote enhanced osteoblast response: chemical composition, crystalline phase, and topography.

As reported on November 5 in the online edition of the *Journal of Biomedical Materials Research Part A* (to appear in print in the December 15 issue), Webster, Rachel L. Price at Purdue, and their colleagues analyzed the osteoblast function depending on the degree of nanometer surface roughness of alumina substrates. The alumina-based materials were chosen for their high osteoblast activity as compared with titanium and etched glass. The researchers used conventional spherical (α-Al_2O_3 spheres, 167 nm), nanophase spherical (δ-Al_2O_3 spheres, 23 nm), and nanofiber (boehmite fiber, 2–4 nm diameter by more than 50 nm long) alumina compounds.

The researchers found that cell adhesion and proliferation results are statistically greater on nanofiber alumina as compared with other compounds. More important, calcium deposition by bone cells significantly increases on both nanoparticulate alumina substrates. They analyzed the influence of the three factors on osteoblast function. The study of the first factor shows that proteins absorb differently on materials with dissimilar chemical composition; the study of the second factor, that the transition alumina (δ- and boehmite phases) may promote an increased cell response compared to the more crystalline alumina phase (α); and the study of the third factor, that a decrease in the grain size to nanometer dimensions translates to an increase in osteoblast function. The researchers demonstrated that nanofiber alumina may offer the potential to ensure sufficient bone ingrowth and therefore to make orthopedic implants more stable.

The researchers concluded that "with knowledge of the influence that chemistry, phase, size, and nanoparticle aspect ratio have on osteoblast function, an ideal material for orthopedic/dental applications may be designed."

EKATERINA A. LITVINOVA

Ferromagnetic Ordering of Pure Organic Compound Occurs Below 1.6 K

Contrary to Heisenberg's proposition that bulk ferromagnetic ordering could only appear in systems with heavy atoms, recent synthesis and characterization of several organic ferromagnets has been reported. Such systems are mainly based on sulfur- or nitrogen-containing organic radicals. A group of researchers from Cambridge University, in cooperation with scientists from CSIC–Universidad de Zaragoza (Spain), CNRS (France), Bunkyo-ku, Japan, and the University of Cardiff (United Kingdom) has discovered a thiazyl-based neutral organic compound that undergoes ferromagnetic ordering below 1.6 K.

As reported in the November 3 issue of *Angewandte Chemie*, Jeremy M. Rawson of Cambridge and colleagues have synthesized and described magnetic properties of the thiazyl-based radical, p-$O_2NC_6F_4CNSSN\bullet$. The radical was obtained by consequent reaction of p-$O_2NC_6F_4CN$ with $Li[N(SiMe_3)_2]$ and SCl_2 in Et_2O solution.

Upon determination of the crystal structure of the radical, the researchers were able to explain the ferromagnetic behavior of the substance. They described the crystal structure as chains of molecules linked through electrostatic $S^{\delta+}\cdots O^{\delta-}$ interactions in the (110) plane with the planes related by means of a 4_1 screw axis along the c-axis. In this case, the molecules form four symmetry-equivalent intermolecular S···N contacts 3.681 Å in length.

The researchers provided detailed magnetic measurements at low temperatures and showed that the compound exhibits Curie–Weiss behavior down to 10 K, while at the temperatures below 1.6 K, it begins to order ferromagnetically. Furthermore, the research team observed magnetic anisotropy in magnetization values along and perpendicular to the [001] axis of a single crystal. Based on crystal structure and previous studies of ferromagnetic properties of analogue thiazyl molecular magnets, the research team concluded that ferromagnetic interactions in the compound are referred to the nearly orthogonal nature of the singly occupied molecular orbitals on neighboring molecules.

ANDREI A. ELISEEV

News of MRS Members/Materials Researchers

Annelise Barron, of the Materials Research Center in Northwestern University, Illinois, was promoted to associate professor with tenure this fall.

Jean Blachère, associate professor emeritus at the University of Pittsburgh, has received the **Albert Victor Bleininger Memorial Award** from the Pittsburgh section of the American Ceramic Society in recognition of his leadership in the ceramics field.

Lynn Boatner of Oak Ridge National Laboratory received the **2003 American Association for Crystal Growth Award** in recognition of his "novel research in the area of crystal growth that has advanced the application of single-crystalline materials and enhanced the appreciation of crystals both scientifically and aesthetically."

Gail J. Brown, principal research physicist in the U.S. Air Force Research Laboratory at Wright-Patterson Air Force Base in Ohio, has received the **Air Force Basic Research Award** for cutting-edge research on superlattice materials for next-generation infrared sensing. The award also recognizes Brown for exemplary leadership in coordinating the research project from computational modeling and growth of the superlattice materials to initial device testing of the new materials' system.

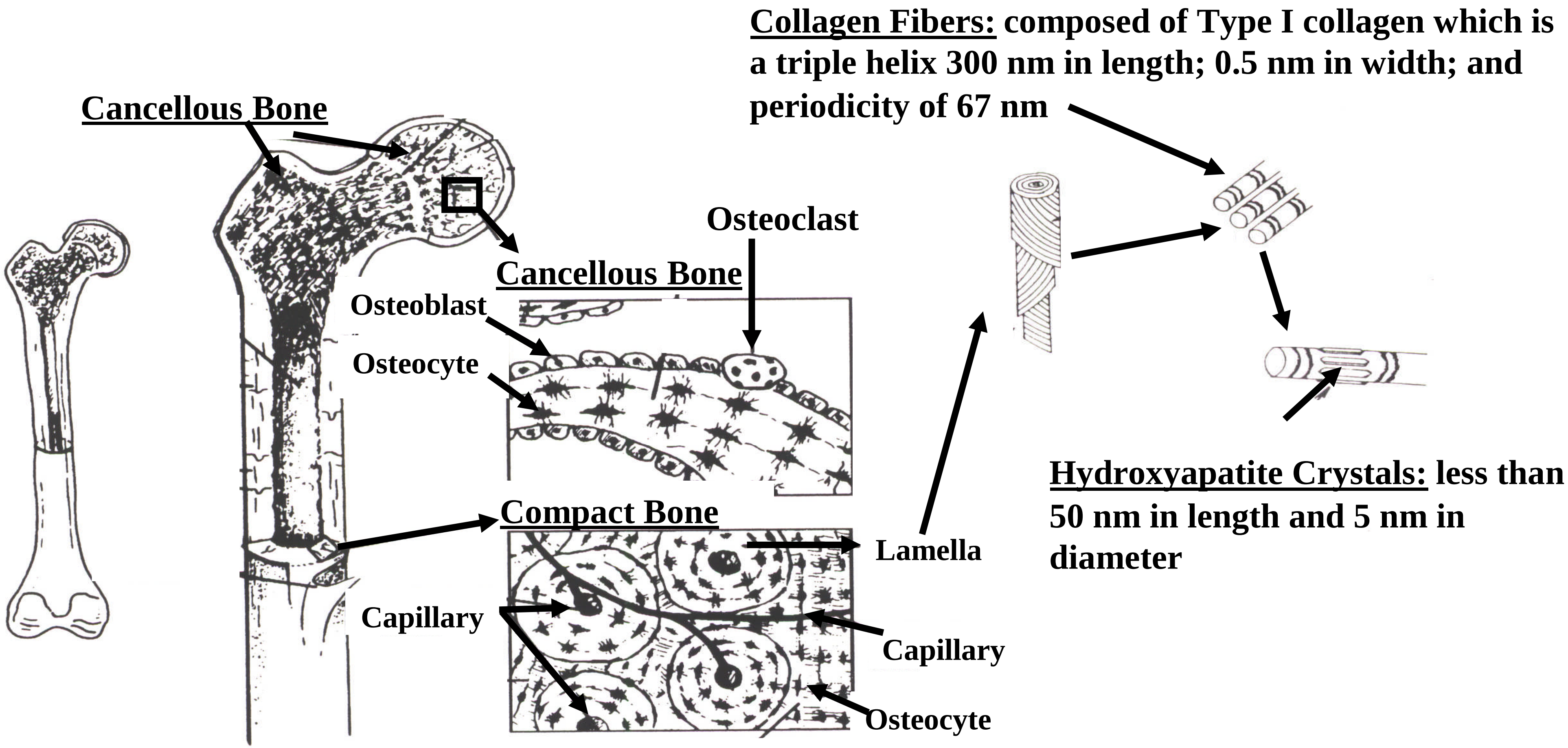
James Wai-Jeung Chan of the Chemical Engineering and Materials Science Department at the University of California, Davis, received the **2003 Zuhair A. Munir Award for Best Doctoral Dissertation** from the UC—Davis College of Engineering for his research on "Confocal Laser Spectroscopy of Glasses Modified by Ultrashort Laser Pulses for Waveguide Fabrication" under the mentorship of Subhash Risbud.

Bai Chunli, vice president of the Chinese Academy of Sciences, has been elected vice president of the Asia Pacific Academy of Materials, a nongovernmental institution aimed at promoting free exchanges of research and development in the field of materials research through international cooperation.

Thomas F. George has been appointed chancellor of the University of Missouri—St. Louis, effective September 1, 2003. Before coming to UM—St. Louis, George

***Materials Research Society Bulletin*, December 2003.**

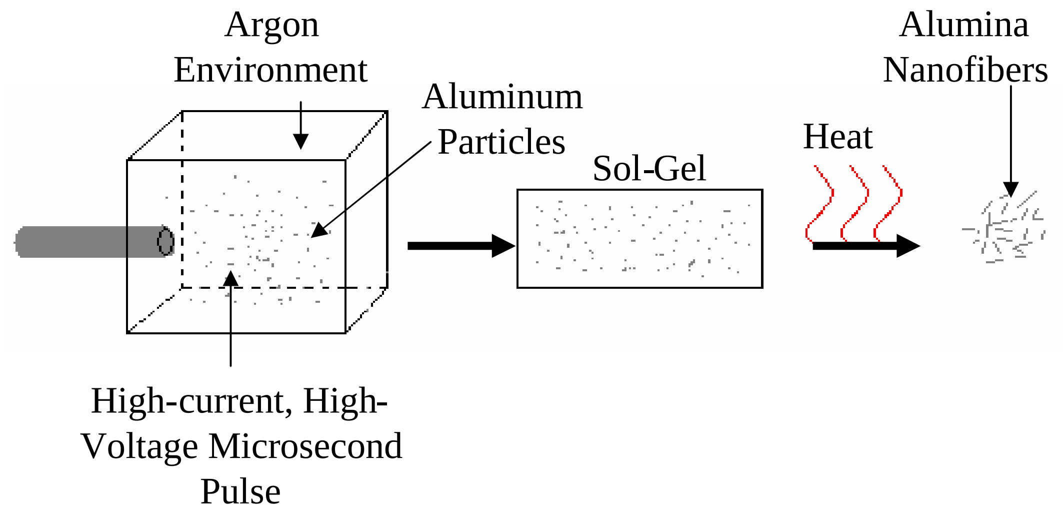
Bone is a Nano-fibered Material



Redrawn and adapted from Fung Biomechanics: Mechanical Properties of Living Tissue, Springer-Verlag, New York, 1993 and Keaveny and Hayes, Bone 7:285, 1993.

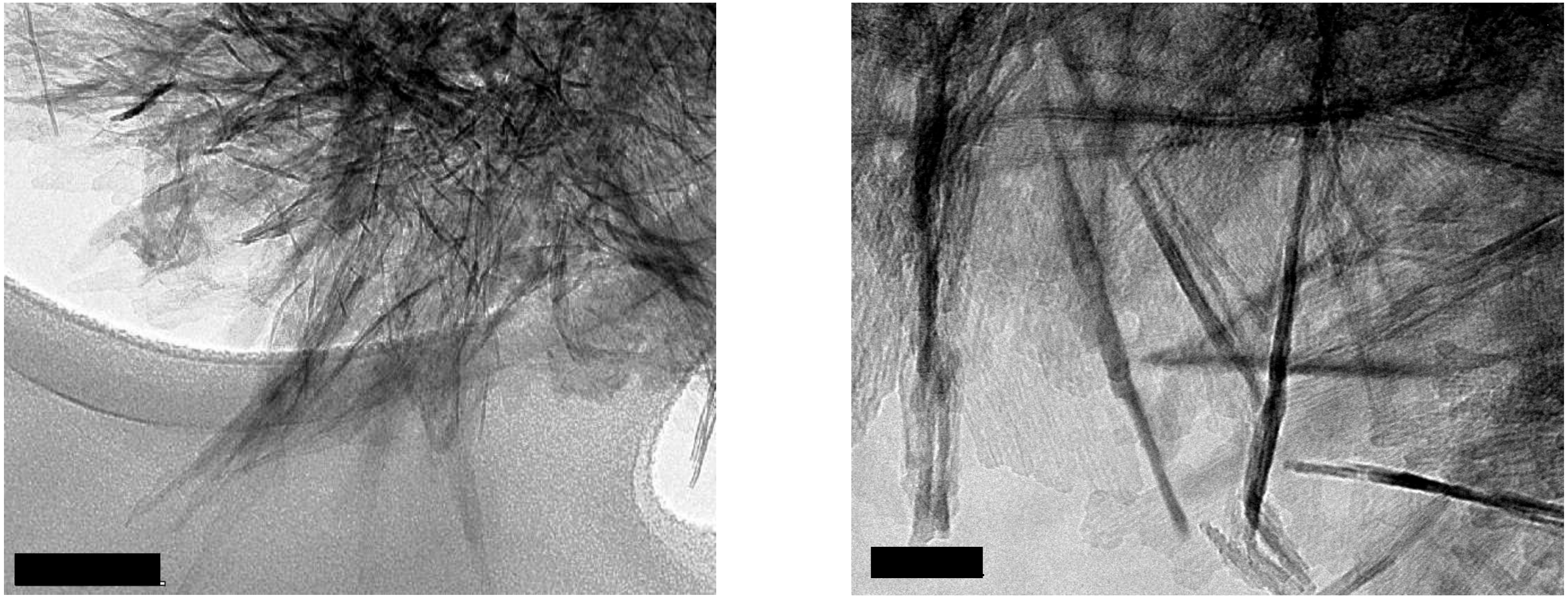
Nanofiber Ceramic Synthesis

- <u>Electro-explosion</u> of aluminum is used to create 100 nm aluminum particles.
  - A microsecond pulse of 100-1000 J is applied to an aluminum wire.
  - The wire explodes when the pulse is discontinued.
  - The exploded fragments pass through an argon environment and become quenched.
- These particles are digested in water to create an aluminum oxide $Al(OH)_3$ sol-gel.
- Subsequent drying of this material (to 400º C) leaves an alumina nano-fiber.



From T. J. Webster, in <u>Nanostructured Biomaterials</u> (H.S. Nalwa, editor), American Scientific Publishers, in press, 2005.

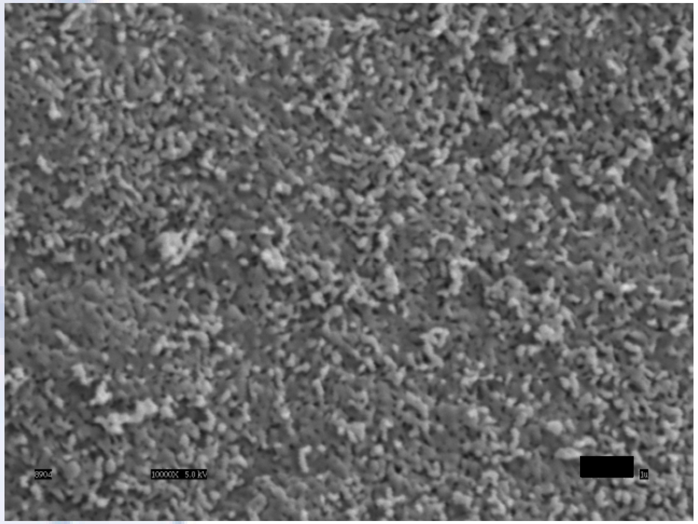
Design of Nano-fiber Ceramics for Orthopedic Implants



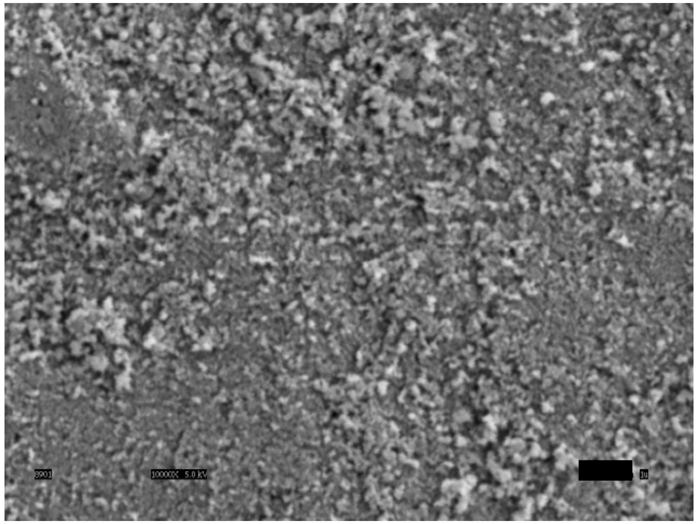
TEM of Individual Alumina Nano-dimensional Fibers
Bar = 100 nm (left) and 20 nm (right).

R.L. Price, K. M. Haberstroh, and T.J. Webster, "Enhanced functions of osteoblasts on nanostructured surfaces of carbon and alumina," ***Medical and Biological Engineering and Computing*** **41:372-375 (2003).**

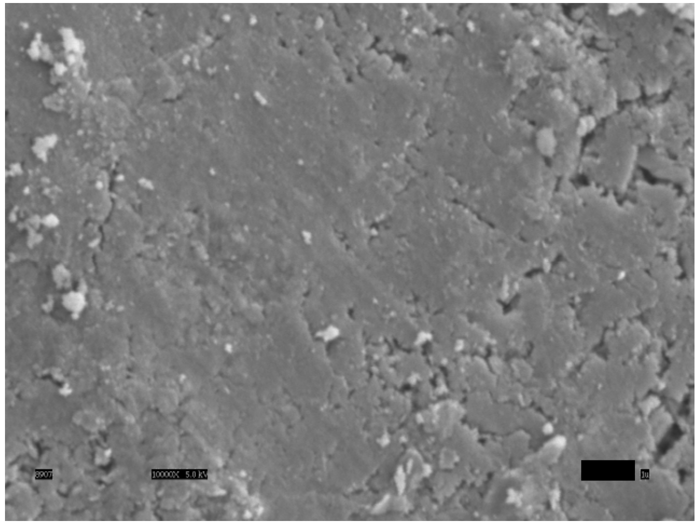
High Magnification Scanning Electron Micrographs of Alumina Substrates



Conventional Alumina



Nano-spherical Alumina

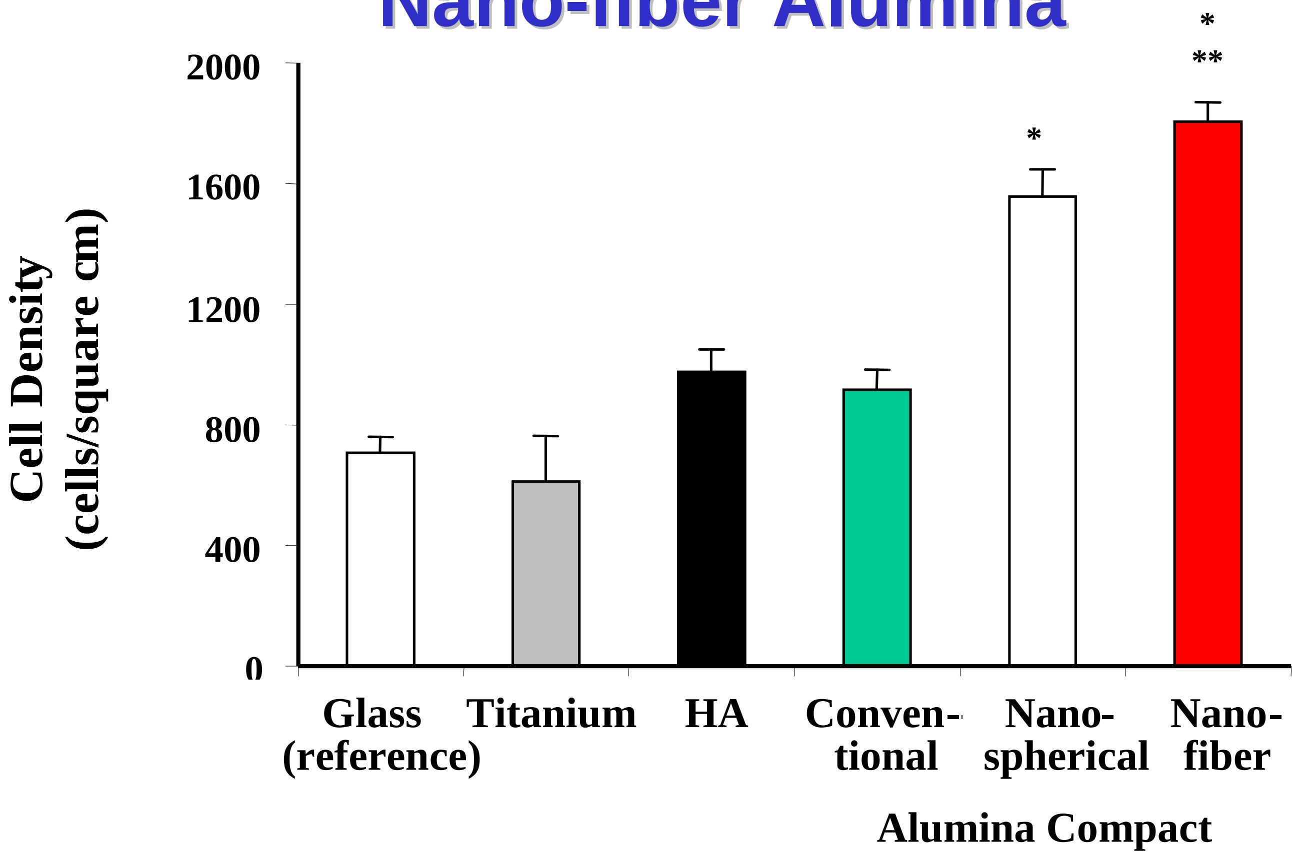


Nano-fiber Alumina

Original Magnification = 10,000X; Bar = 1 μm.

R.L. Price, L.G. Gutwein, L. Kaledin, F. Tepper, and T.J. Webster,
***Journal of Biomedical Materials Research* 67A:1284-1293 (2003).**

Enhanced Osteoblast Adhesion on Nano-fiber Alumina

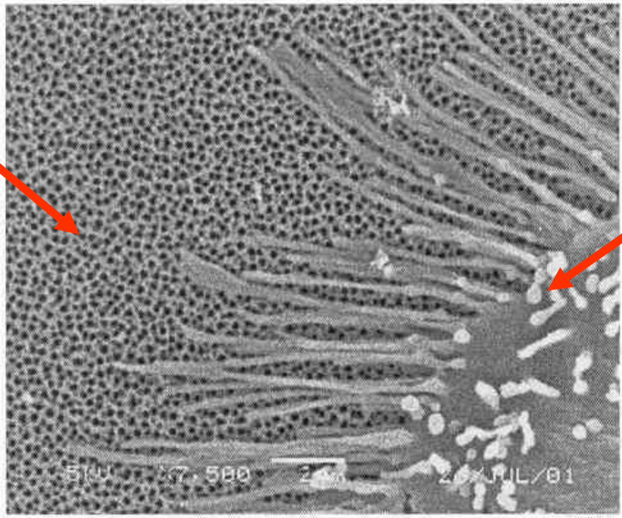


Culture medium = DMEM supplemented with 10% fetal bovine serum. Seeding density = 2,500 cells/cm^2. Culture time = 2 hrs. Values are mean +/- SEM; n = 3; * *p* < 0.01 (compared to titanium); ** *p* < 0.05 (compared to nano-spherical alumina).

R.L. Price, L.G. Gutwein, L. Kaledin, F. Tepper, and T.J. Webster,
***Journal of Biomedical Materials Research* 67A:1284-1293 (2003).**

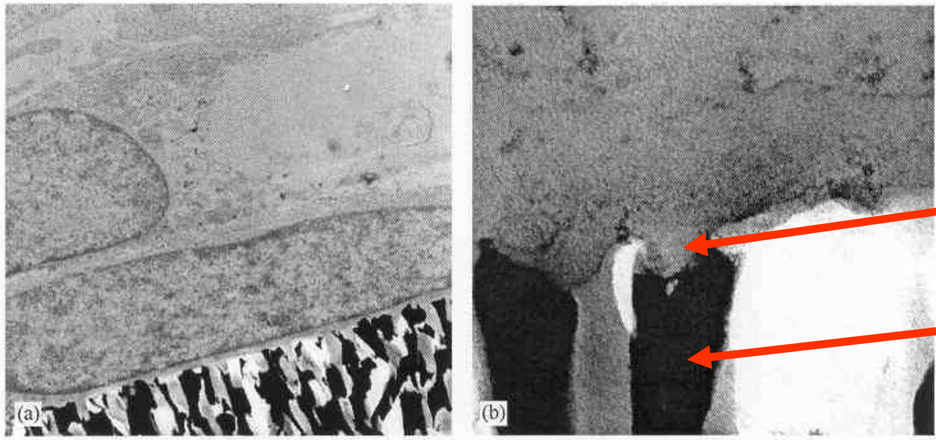
Other Novel Nano-Formulations of Alumina

Nanoporous Alumina



Osteoblast filipodia

Studies have shown superior osteoblast functions leading to increased in vitro new bone synthesis on nano-porous alumina.



Osteoblast filipodia

Nanoporous Alumina

Karlsson et al, Biomaterials 24 (2003) 3039-3046.

PART I (cont.)

BONE: Carbon Nanofibers

OF NOTE

in animals not receiving the ion. The detrimental effects lessened but persisted at arsenite doses up to 5.0 mg/kg, beyond which arsenic's toxicity would be too high for therapeutic purposes.

Because it's difficult to precisely regulate blood levels of arsenic in patients, these results present daunting obstacles to expanding medical uses of the substance, says Barchowsky. He and his colleagues at Dartmouth Medical School in Hanover, N.H., and the University of Oklahoma in Oklahoma City report their findings in the December 2003 *Toxicological Sciences*. —B.H.

EARTH SCIENCE

Warming climate may slam many species

Expected increases in global temperature could eradicate from a sixth to a half of the plant and animal species across large areas of the globe, scientists say.

Climate change over the past 30 years has produced significant shifts in the population sizes and the geographical distributions of many species, says Chris D. Thomas, an ecologist at the University of Leeds in England. He and his colleagues recently used mapping techniques to discern population and distribution trends of 1,103 selected plant and animal species that live in parts of Mexico, Australia, South Africa, Europe, and the Amazon rain forest. The areas studied account for 20 percent of the Earth's land surface.

If the average global temperature rises between 0.8°C and 1.7°C by 2050—the minimum expected change, say the researchers—13 percent of the species studied could become extinct or so reduced in number that they couldn't recover. Those figures assume that all of the plants and animals would be free to move to suitable habitats in the new climatic regime. If species couldn't migrate because of factors such as habitat fragmentation, then up to 31 percent of the species studied could be wiped out.

For global temperature increases greater than 2°C, the picture is grimmer: About one-third of those species that move to more suitable settings could still succumb, and a whopping 52 percent could eventually become extinct if no migration were to occur.

Assuming the species in the study are representative of most plants and animals in the areas studied, even the least deadly cases of climate change could wipe out more than 1 million species, the researchers warn in the Jan. 8 *Nature*. —S.P.

MATERIALS SCIENCE

Nanotube implants could aid brain research

To probe the mysteries of the mind and restore brain function in patients suffering from trauma or disease, researchers have been developing various implants that can record and stimulate neural activity. Because these probes are typically made of silicon, however, scar tissue forms on such an implant, creating a barrier between the device and brain cells.

Implants made from electrically conducting carbon nanotubes could offer a safer and more effective alternative to silicon, according to a group of biomedical engineers at Purdue University in West Lafayette, Ind. Led by Thomas Webster, the researchers fabricated a new implant material by mixing multiwalled carbon nanotubes—sheets of graphite rolled into concentric cylinders—with a polymer already used in some surgical implants.

To test the suitability of the material for implants, Webster's team placed coin-size samples of the polymer-nanotube material in petri dishes with either astrocytes, which are cells that form scar tissue, or nerve cells. The material not only significantly reduced the formation of scar tissue, but also stimulated contact with nerve cells by inducing them to grow fingerlike extensions. The findings appear in the January *Nanotechnology*.

The implant developers attribute the cell-morphing and scar-shunning effect to the material having no more than nanometer-size bumps, which mimic the natural surfaces of proteins and tissues. Conventional probes typically have larger defects, which the body perceives as foreign. —A.G.

NEUROSCIENCE

Hot or cold? Debate on protein heats up

The pungency of wasabi, horseradish, brussels sprouts, and mustards comes from compounds called isothiocyanates. Applying those same compounds to a person's skin can cause pain and inflammation.

Isothiocyanates activate pain-signaling neurons by triggering a cell-surface protein that lets ions into cells, David Julius of University of California, San Francisco and his colleagues report in an upcoming *Nature*. Julius' group had previously shown that capsaicin, the compound that gives chili peppers their spicy kick, activates a different but related ion channel (*SN: 11/8/97, p. 297*). Curiously, the active ingredient in marijuana triggers the same ion channel that the isothiocyanates do, the researchers found.

In another twist, Julius and his colleagues tried but failed to confirm another group's claim that this protein also enables some nerve cells to respond to painfully cold temperatures (*SN: 5/10/03, p. 301*).

"We don't really know why our results differ," Julius says. Studies of sensory nerves from mice genetically engineered to lack the protein may resolve its roles, he adds. —J.T.

INFECTIOUS DISEASES

Insect receptor for sweat creates buzz

In many places, the drone of a nearby mosquito is more than annoying—it's dangerous. These insects transmit a variety of diseases, including yellow fever and malaria.

Scientists have now identified a protein that certain mosquitoes use to home in on human skin. This receptor, which resides on the surface of olfactory cells, senses 4-methyphenol, a molecule found in human sweat. John R. Carlson of Yale University and his colleagues reveal the finding in the Jan. 15 *Nature*.

In 1999, Carlson's group and another research team reported that studies of the common fruit fly had uncovered insect odor receptors for the first time (*SN: 4/10/99, p. 237*). In the new work, Carlson and his colleagues took the gene for a putative odor receptor in *Anopheles* mosquitoes, the world's most common carrier of malaria, and inserted it into fruit fly olfactory cells that are typically unresponsive to 4-methyphenol. The engineered cells exhibited a strong response to the compound, a good indication that the receptor is actually a means by which mosquitoes home in on sweat.

The receptor is made only in the olfactory tissue of female mosquitoes, which are the ones that feed on blood meals from people.

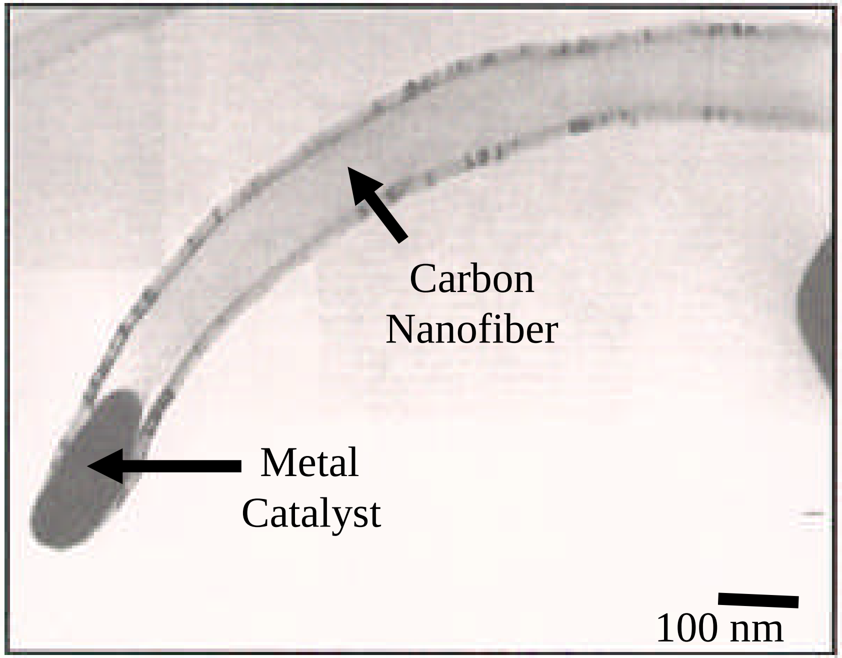
New mosquito repellents could be developed from compounds that block the receptor, or 4-methyphenol might work as a lure that could divert the insects from people, the researchers suggest. Indeed, 4-methyphenol has already been used to trap disease-carrying tsetse flies.

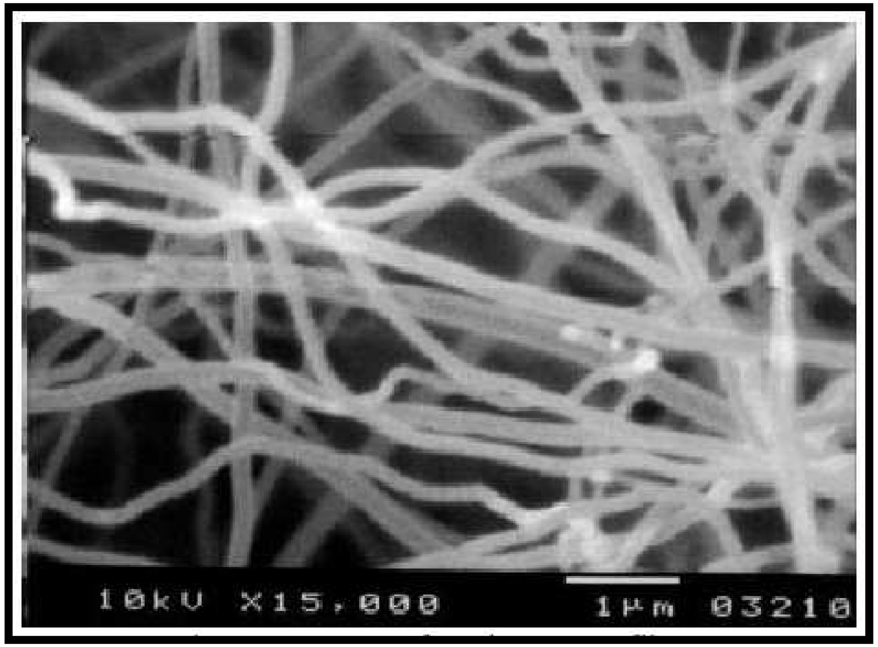
"Mosquitoes are likely to use multiple cues in seeking their human hosts, and the best repellents may be cocktails of multiple compounds," says Carlson. "We're now actively looking at other mosquito receptors to determine whether they respond to other human-sweat odorants." —J.T

Science News, January 24, p. 62, 2004.

Carbon Nanofiber Synthesis

- **Chemical Vapor Deposition**
  - A metal catalyst acts as a template for carbon deposition from a hydrocarbon gas environment.
  - More time in the hydrocarbon environment = larger fiber diameter.





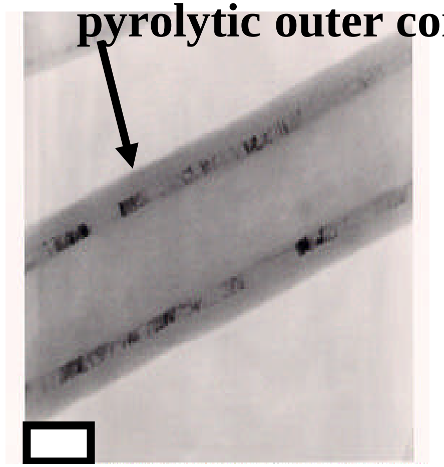
J. U. Ejiofor, M. C. Waid, J. L. McKenzie, R. L. Price, and T. J. Webster, *Nanotechnology* 15:48-54 (2004).

Design of Carbon Nanofibers for Orthopedic Implants

Fiber	Fiber Diameter (nm)	Surface Energy
Nanophase w/ pyrolytic outer core	100	Low
Conventional w/ pyrolytic outer core	200	Low
Nanophase w/o pyrolytic outer core	60	High
Conventional w/o pyrolytic outer core	125	High

K. L. Elias, R. L. Price, and T. J. Webster, *Biomaterials* 23: 3279-3287 (2002).

pyrolytic outer core



no pyrolytic outer core

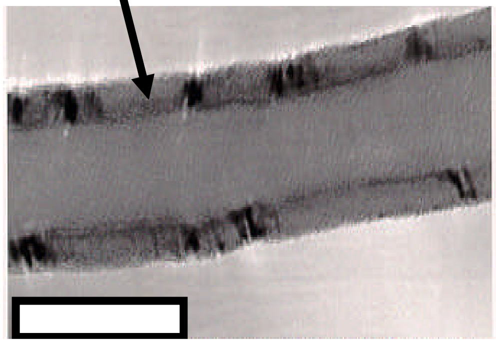
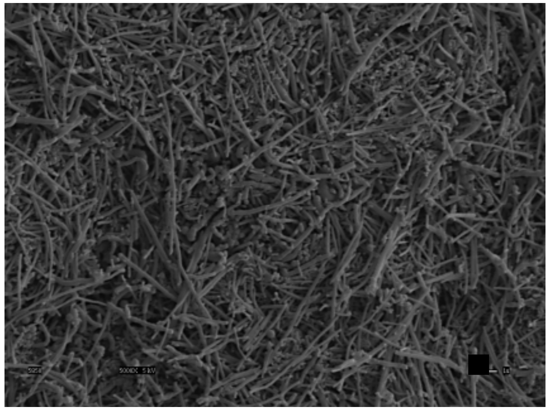
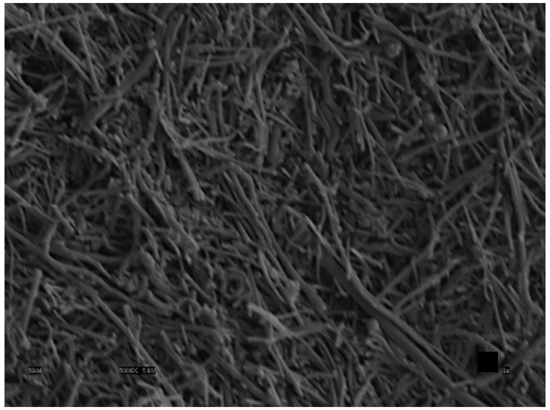


Figure: TEM of Individual Carbon Nano-dimensional Fibers
Bar = 100 nm.

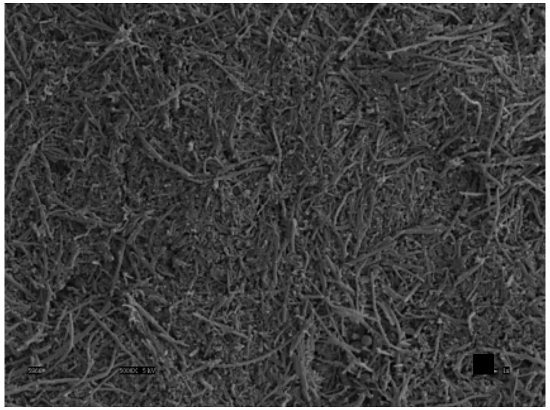
Scanning Electron Micrographs of Carbon Fiber Compacts



Nanophase w/Low Surface Energy

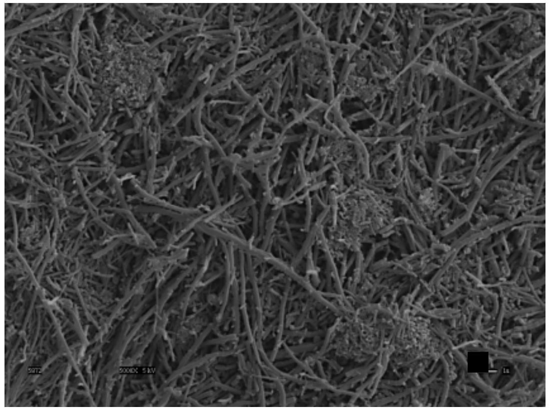


Conventional w/Low Surface Energy



Nanophase w/High Surface Energy

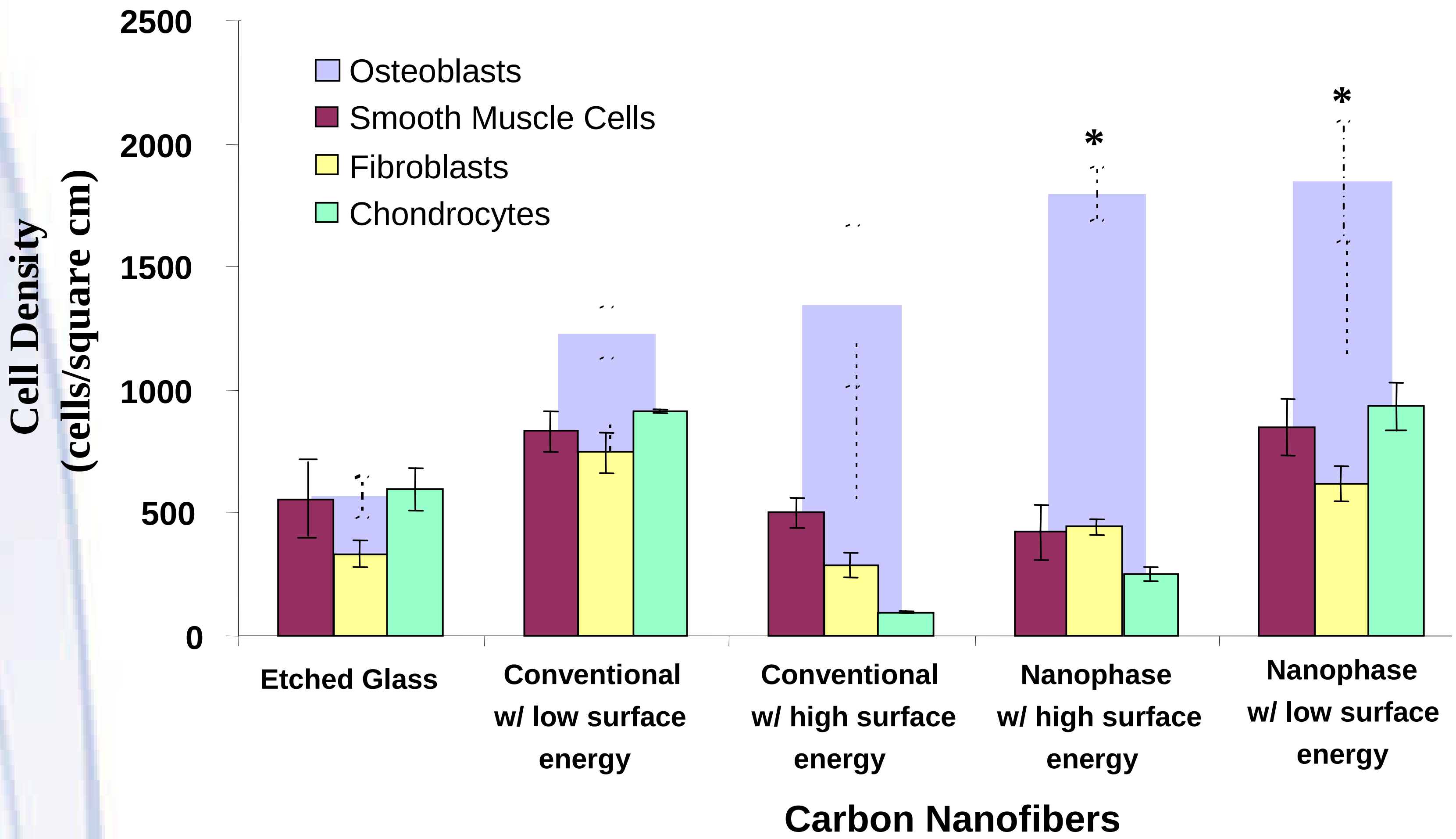
Bar = 1 μm.



Conventional w/High Surface Energy

R. L. Price, M. C. Waid, K. M. Haberstroh, and T. J. Webster, "Increased, select bone cell adhesion on formulations containing carbon nanofibers," *Biomaterials*, 24(11): 1877 – 1887, 2003.

Enhanced, Select Osteoblast Adhesion on Carbon Nanofibers

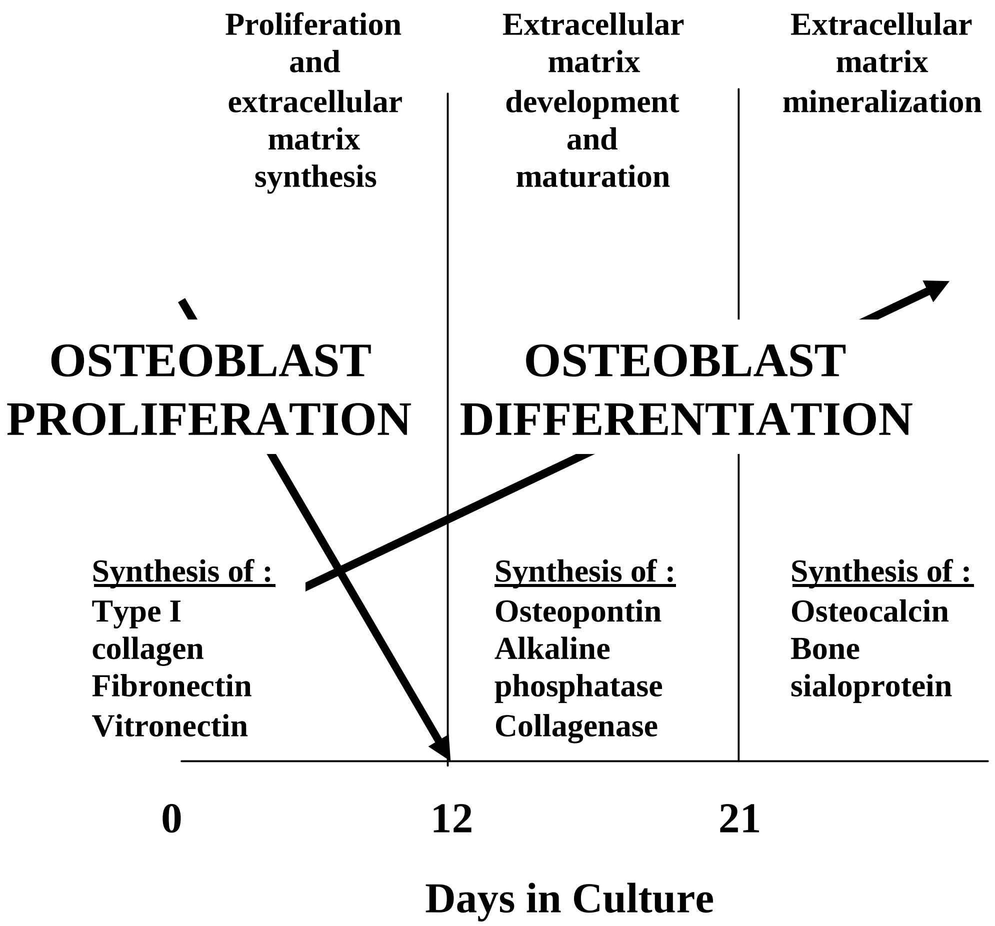


Values are mean +/-SEM; n=3; * *p*<0.10 (compared to conventional counterpart).

R. L. Price, M. C. Waid, K. M. Haberstroh, and T. J. Webster,
***Biomaterials*, 24(11): 1877 – 1887, 2003.**

Enhanced Adhesion Translates into Increased Subsequent Functions

Stages of Osteoblast Differentiation



T. J. Webster, in Advances in Chemical Engineering Vol. 27, Academic Press, NY, pgs. 125-166, 2001.