

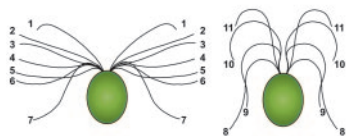
In This Issue

- 11963 Intact biological motors for moving microscale loads
 11989 Casimir force affected by metallic skin depth
 12153 Improving graft survival in islet transplantation
 12177 Efficient siRNA delivery to metastatic tumors
 12265 Yeast gene enhances recombination in *Arabidopsis*

APPLIED PHYSICAL SCIENCES

Intact biological motors for moving microscale loads

Douglas Weibel *et al.* report the utilization of the unicellular, biflagellated algae *Chlamydomonas reinhardtii* to harness the power produced by its biological motors. The authors exploited the surface chemistry of the algal cell wall to attach polystyrene beads (1–6 μm in diameter) to the cells ($\approx 10 \mu\text{m}$ in diameter).

Movement of flagella of *Chlamydomonas reinhardtii*.

These modified cells could swim at velocities as high as 100–200 $\mu\text{m}/\text{s}$, which is roughly the speed of unmodified cells. The cells could then be steered via phototaxis to carry the bead loads in microfluidic systems: when light-emitting diodes at the end of a 2- to 3-cm-long microfluidic channel were turned on and off, cells carrying beads swam back and forth repeatedly along the channel. To detach loads from cells, a photocleavable group was incorporated into peptides decorating the beads. Ultraviolet irradiation released the loads, and the cells could continue to be guided by phototaxis. The use of intact biological nanomotors in living cells may be a more practical strategy for their use compared with separating them from the cell and using them in isolation, the authors say. — R.N.

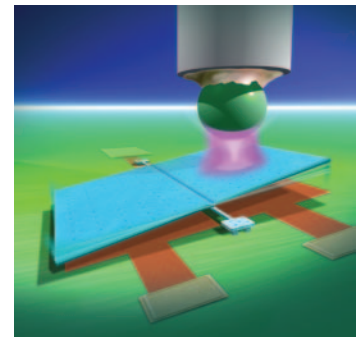
“Microoxen: Microorganisms to move microscale loads” by Douglas B. Weibel, Piotr Garstecki, Declan Ryan, Willow R. DiLuzio, Michael Mayer, Jennifer E. Seto, and George M. Whitesides (see pages 11963–11967)

PHYSICS

Casimir force affected by metallic skin depth

Mariangela Lisanti *et al.* demonstrate that the Casimir force between metallic surfaces is significantly smaller for thin metal-

lic coatings than for thick, bulk-like films. The Casimir force is a measure of the quantum attraction of two electrically neutral, metallic plates kept parallel to each other in a vacuum. Lisanti *et al.* coated a polystyrene sphere with a 90-Å film of palladium, mounted it in a vacuum chamber, and placed the gold-coated top plate of a micromachined torsional balance submicron distances away. The authors evacuated the chamber and measured the rotation angle of the balance induced by the Casimir attraction as a function of the distance between the surfaces, and then coated the sphere with an additional 2,000 Å of palladium to re-measure attraction. The magnitude of the force was significantly reduced for the thin film when compared with the thick coating. However, a theoretical calculation using the Lifshitz equation overestimated the force for the thin metallic film by up to 25%. The authors say that this discrepancy was caused by approximations in the dielectric function for thin materials and to the roughness of the two surfaces. — F.A.



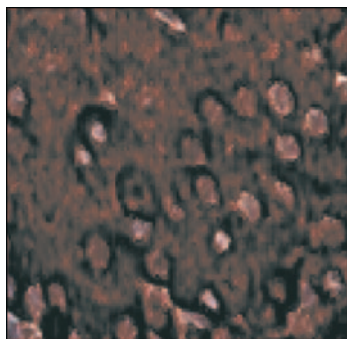
Micromechanical balance to measure Casimir forces between metallized sphere and thick gold layer.

“Observation of the skin-depth effect on the Casimir force between metallic surfaces” by Mariangela Lisanti, Davide Iannuzzi, and Federico Capasso (see pages 11989–11992)

IMMUNOLOGY

Improving graft survival in islet transplantation

Eli Lewis *et al.* report that therapy with human $\alpha 1$ -antitrypsin (AAT), the major serum serine-protease inhibitor, prolonged islet of Langerhans graft survival in diabetic mice. Islet transplantation, together with steroid-free, nondiabetogenic immunosuppressive therapy, has been used to treat patients with type 1 diabetes. However, such treatments can lead to increased risk



Allogeneic islet graft in AAT-treated mice.

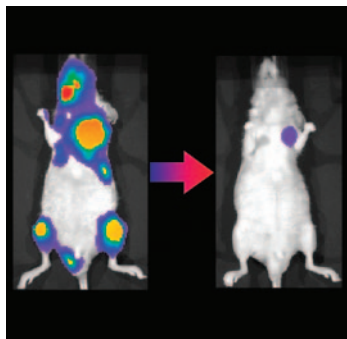
displayed steady intragraft insulin production throughout treatment. The authors examined several islet responses to IL-1 β /IFN- γ stimulation *in vitro* to pinpoint the mechanisms of prolonged survival: AAT-treated islets released 36% less nitric oxide, 82% less macrophage inflammatory protein 1 α , and 63% less surface MHC class II molecules. AAT treatment also decreased allogeneic fibroblast-elicited natural killer cell influx by 89%, CD3⁺ cell influx by 44%, and thioglycolate-elicited neutrophil emigration by 66%. These findings suggest AAT may be beneficial as adjunctive therapy in patients undergoing islet transplantation. — N.Z.

“ α 1-antitrypsin monotherapy prolongs islet allograft survival in mice” by Eli C. Lewis, Leland Shapiro, Owen J. Bowers, and Charles A. Dinarello (see pages 12153–12158)

MEDICAL SCIENCES

Efficient siRNA delivery to metastatic tumors

Fumitaka Takeshita *et al.* report suppression of growth of bone-metastatic prostate tumors by using atelocollagen to deliver small interfering RNAs (siRNAs). Previous research has shown that siRNAs can specifically reduce the expression of genes in certain types of cancers, but siRNA delivery strategies, such as viral- or lipid-based vectors, have had varied success and are



Tumor growth suppression in mice treated with siRNA/atelocollagen complex.

of hyperlipidemia and hypertension, and long-term studies demonstrate that islet viability is impaired. Lewis *et al.* examined an alternate treatment strategy of monotherapy with clinical-grade AAT in transplanted allogeneic diabetic mice. Islet graft survival was shown to last until the development of anti-AAT antibodies, whereas control mice rejected the grafts after 10 days. AAT-treated mice also

displayed steady intragraft insulin production throughout treatment. The authors examined several islet responses to IL-1 β /IFN- γ stimulation *in vitro* to pinpoint the mechanisms of prolonged survival: AAT-treated islets released 36% less nitric oxide, 82% less macrophage inflammatory protein 1 α , and 63% less surface MHC class II molecules. AAT treatment also decreased allogeneic fibroblast-elicited natural killer cell influx by 89%, CD3⁺ cell influx by 44%, and thioglycolate-elicited neutrophil emigration by 66%. These findings suggest AAT may be beneficial as adjunctive therapy in patients undergoing islet transplantation. — N.Z.

“ α 1-antitrypsin monotherapy prolongs islet allograft survival in mice” by Eli C. Lewis, Leland Shapiro, Owen J. Bowers, and Charles A. Dinarello (see pages 12153–12158)

prone to activating deleterious immune responses. Atelocollagen is a highly purified type I collagen that is modified to have low immunogenicity.

Takeshita *et al.* injected a bioluminescent human prostate carcinoma cell line into immunodeficient mice, causing metastatic lesions in the thorax, jaws, and legs. The mice were then treated with a luciferase siRNA/atelocollagen complex, and bioluminescence decreased by up to 90%,

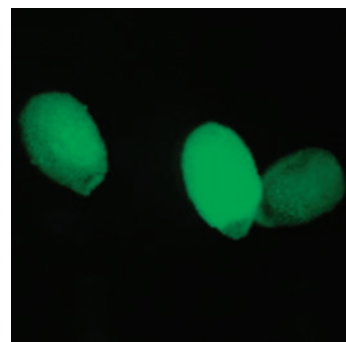
whereas it increased in mice treated with atelocollagen alone or a control siRNA/atelocollagen complex. The atelocollagen system was used to deliver siRNAs of EZH2 (gene overexpressed in metastatic prostate cancer) and p110 α (gene regulating cell survival, proliferation, and migration) to the metastatic animals. A significant decrease in metastasis was observed in the whole bodies of the treated animals. In addition, siRNA/atelocollagen treatment did not elicit an interferon immune response in the mice. — F.A.

“Efficient delivery of small interfering RNA to bone-metastatic tumors by using atelocollagen *in vivo*” by Fumitaka Takeshita, Yoshiko Minakuchi, Shunji Nagahara, Kimi Honma, Hideo Sasaki, Kotaro Hirai, Takumi Teratani, Nachi Namatame, Yusuke Yamamoto, Koji Hanai, Takashi Kato, Akihiko Sano, and Takahiro Ochiya (see pages 12177–12182)

PLANT BIOLOGY

Yeast gene enhances recombination in *Arabidopsis*

Hezi Shaked *et al.* increased homologous DNA integration frequency in *Arabidopsis* by an order of magnitude through heterologous expression of the yeast *RAD54* gene. Specific gene targeting is an inefficient process in many eukaryotes because random DNA integration greatly exceeds homologous integration. The chromosomal enzymes that are rate-limiting in homologous integration are not known. Shaked *et al.* grew transgenic *Arabidopsis* plants expressing the *RAD54* gene, which facilitates the invasion of a homologous template via chromatin remodeling in yeast. The authors constructed



Arabidopsis seeds expressing homologously integrated GFP.

a vector for homologous recombination targeting GFP to the endogenous *Cruciferin* gene in *Arabidopsis*, which expresses a seed-specific storage protein. Seeds expressing GFP were identified by fluorescence, and gene-targeting events were 62-fold higher in *RAD54*-expressing plants versus wild type. Sequencing confirmed the precise insertion of GFP on both sides of the integration borders. To investigate whether the targeted allele was transmitted in the germ line, the authors self-pollinated plants grown from GFP seeds and observed that \approx 75% of the next-generation seeds were fluorescent, suggesting normal gamete transmission of the GFP-containing allele. In plants homozygous for the targeted allele, the wild-type allele was missing, indicating that gene replacement had occurred. — F.A.

“High-frequency gene targeting in *Arabidopsis* plants expressing the yeast *RAD54* gene” by Hezi Shaked, Cathy Melamed-Bessudo, and Avraham A. Levy (see pages 12265–12269)