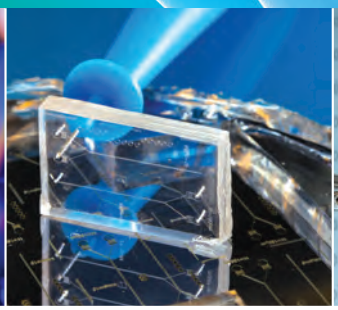
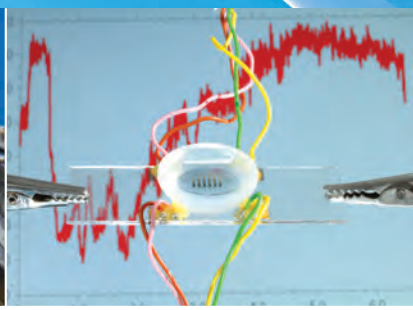
CEA
Life Sciences
Division

Highlights 2014





Bioenergy

Radiobiology Toxicology

Diagnostic and therapeutic innovations

Molecular and cellular mechanisms of living organisms

Technological developments

FROM RESEARCH TO INDUSTRY
cea

CEA, the French Atomic Energy and Alternative Energies Commission

Highlights
2014

Bioenergy

Biofuels Catalysis Algae
Green chemistry Plants Metabolic pathways
Genomic and metagenomic studies of biodiversity
Catalysis Bio-inspired processes
Enzymes structure Synthons Biofuels Plants
Synthons Bio-inspired processes Bio-engineering
Hydrogen Genomic and metagenomic studies of biodiversity
Enzymes structure Metabolic pathways
Green chemistry Bio-engineering Algae Hydrogen

Science

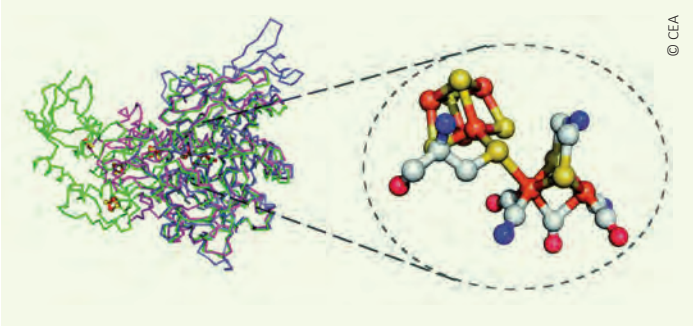
■ **Electronic structure of the oxygen-evolving complex in photosystem II prior to O-O bond formation**
Cox N, Retegan M, Neese F, Pantazis DA, Boussac A, Lubitz W.
Science, 2014, 345 (6198), 804-808

Nature Chemistry

■ **The oxidative inactivation of FeFe hydrogenase reveals the flexibility of the H-cluster**
Fourmond V, Greco C, Sybirna K, Baffert C, Wang PH, Ezanno P, Montefiori M, Bruschi M, *et al.*
Nat. Chem., 2014, 6 (4), 336-342

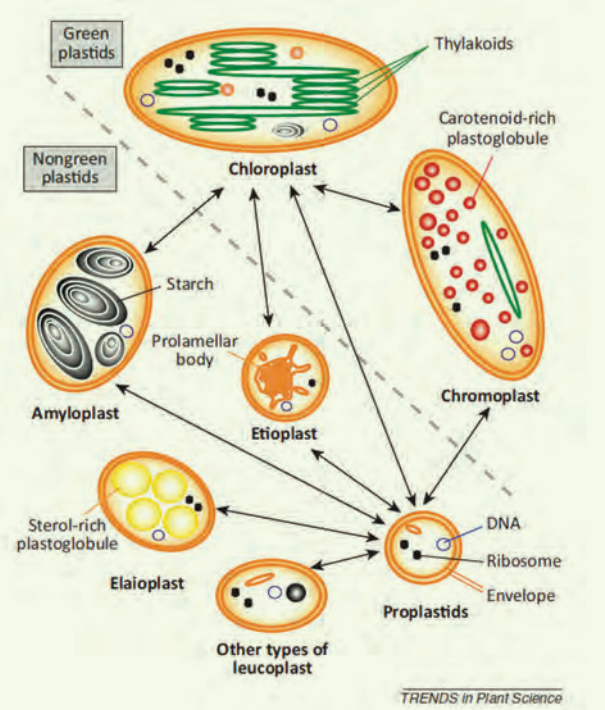
Energy & Environmental Science

■ **FeFe hydrogenase reductive inactivation and implication for catalysis**
Hajj V, Baffert C, Sybirna K, Meynial-Salles I, Soucaille P, Bottin H, Fourmond V, Leger C.
Energy Environ. Sci., 2014, 7, 715-719



The backbones of the FeFe hydrogenases from different bacteria and green alga with a model of the H-cluster. Hajj V, *et al.* Energy Environ. Sci., 2014.

■ **Toward the rational benchmarking of homogeneous H-2-evolving catalysts**
Artero V, Saveant JM.
Energy Environ. Sci., 2014, 7, 3808-3814



Plastid interconversion in angiosperms. Botte CY, Marechal E. Trends Plant Sci., 2014.

Organometallics

■ **New Systematic Route to Mixed-Valence Triiron Clusters Derived from Dinuclear Models of the Active Site of [Fe-Fe]-Hydrogenases**
Beaume L, Clemancey M, Blondin G, Greco C, Petillon FY, Schollhammer P, Talarmin J.
Organometallics, 2014, 33 (22), 6290-6293

Trends in Plant Sciences

■ **Plastids with or without galactoglycerolipids**
Botte CY, Marechal E.
Trends Plant Sci., 2014, 19 (2), 71-78

Nature Chemical Biology

■ **Revealing the hidden functional diversity of an enzyme family**
Bastard K, Smith AAT, Vergne-Vaxelaire C, Perret A, Zaparucha A, De Melo-Minardi R, Mariage A, Boutard M, *et al.*
Nat. Chem. Biol., 2014, 10 (1), 42-9

Progress in Lipid Research

- **Evolution of galactoglycerolipid biosynthetic pathways - From cyanobacteria to primary plastids and from primary to secondary plastids**

Petroutsos D, Amiar S, Abida H, Dolch LJ, Bastien O, Rebeille F, Jouhet J, Falconet D, *et al.*
Prog. Lipid Res., 2014, 54, 68-85

Coordination Chemistry Reviews

- **Mimicking hydrogenases: From biomimetics to artificial enzymes**

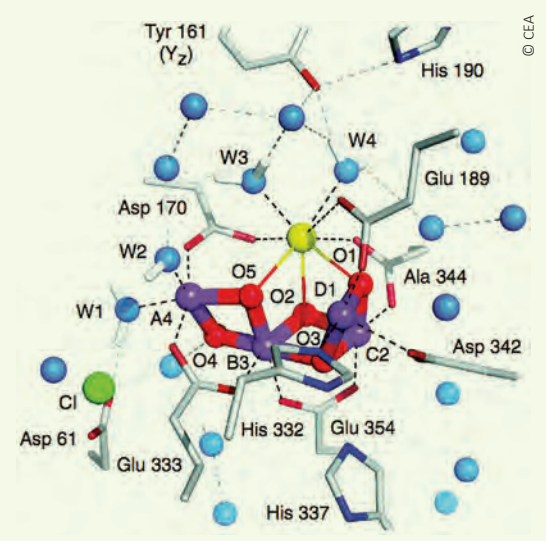
Simmons TR, Berggren G, Bacchi M, Fontecave M, Artero V.
Coord. Chem. Rev., 2014, 270, 127-150

Journal of the American Chemical Society

- **ATP Binding and Aspartate Protonation Enhance Photoinduced Electron Transfer in Plant Cryptochrome**

Cailliez F, Muller P, Gallois M, de la Lande A.
J. Am. Chem. Soc., 2014, 136 (37), 12974-12986

Phytotechnology plateform at the Institute of Environmental Biology and Biotechnology in Cadarache.



The water-oxidizing complex in photosystem II. Nilsson H, *et al.* Nat. Commun., 2014.

- **Triggering the Generation of an Iron(IV)-Oxo Compound and Its Reactivity toward Sulfides by Ru-II Photocatalysis**

Company A, Sabenya G, Gonzalez-Bejar M, Gomez L, Clemancey M, Blondin G, Jasniewski AJ, Puri M, *et al.*
J. Am. Chem. Soc., 2014, 136 (12), 4624-4633

Angewandte Chemie International Edition

- **Photocatalytic Hydrogen Production using Polymeric Carbon Nitride with a Hydrogenase and a Bioinspired Synthetic Ni Catalyst**

Caputo CA, Gross MA, Lau VW, Cavazza C, Lotsch BV, Reisner E.
Angew. Chem.-Int. Edit., 2014, 53 (43), 11538-11542

Nature Communication

- **Substrate-water exchange in photosystem II is arrested before dioxygen formation**

Nilsson H, Rappaport F, Boussac A, Messinger J.
Nat. Commun., 2014, 5, e4305

Proceedings of the National Academy of Sciences of the United States of America

- **Chloroplast remodeling during state transitions in *Chlamydomonas reinhardtii* as revealed by noninvasive techniques in vivo**

Nagy G, Unnep R, Zsiros O, Tokutsu R, Takizawa K, Porcar L, Moyet L, Petroutsos D, *et al.*
Proc. Natl. Acad. Sci. U. S. A., 2014, 111 (13), 5042-5047

Highlights 2014

Bioenergy

■ **Heterocyst-specific flavodiiron protein Flv3B enables oxic diazotrophic growth of the filamentous cyanobacterium *Anabaena* sp. PCC 7120**

Ermakova M, Battchikova N, Richaud P, Leino H, Kosourov S, Isojarvi J, Peltier G, Flores E, *et al.*

Proc. Natl. Acad. Sci. U. S. A., 2014, 111 (30), 11205-11210

Culture of *cyanobacteria*, also called blue-green algae. Ermakova M, *et al.* Proc. Natl. Acad. Sci. U. S. A., 2014.

■ **Molecular basis for Auxin Response Factor protein interaction and the control of auxin response repression**

Korasick DA, Westfall CS, Lee SG, Nanao MH, Dumas R, Hagen G, Guilfoyle TJ, Jez JM, Strader LC.

Proc. Natl. Acad. Sci. U. S. A., 2014, 111 (14), 5427-5432

Plant Cell

■ **Combined Increases in Mitochondrial Cooperation and Oxygen Photoreduction Compensate for Deficiency in Cyclic Electron Flow in *Chlamydomonas reinhardtii***

Dang KV, Plet J, Tolleter D, Jokel M, Cuine S, Carrier P, Auroy P, Richaud P, *et al.*

Plant Cell, 2014, 26 (7), 3036-3050

■ **Structural and Functional Modularity of the Orange Carotenoid Protein: Distinct Roles for the N- and C-Terminal Domains in Cyanobacterial Photoprotection**

Leverenz RL, Jallet D, Li MD, Mathies RA, Kirilovsky D, Kerfeld CA.

Plant Cell, 2014, 26 (1), 426-437

■ **The Cyanobacterial Photoactive Orange Carotenoid Protein Is an Excellent Singlet Oxygen Quencher**

Sedoud A, Lopez-Igual R, Rehman AU, Wilson A, Perreau F, Boulay C, Vass I, Krieger-Liszkay A, Kirilovsky D.

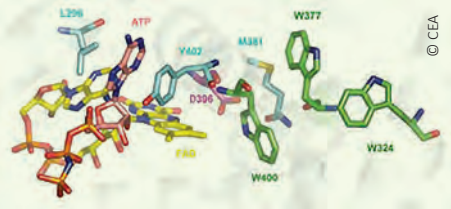
Plant Cell, 2014, 26 (4), 1781-1791

Scientific Reports

■ **ATP Binding Turns Plant Cryptochrome Into an Efficient Natural Photoswitch**

Müller P, Bouly JP, Hitomi K, Balland V, Getzoff ED, Ritz T, Brettel K.

Sci. Rep., 2014, 4, 5175



The photoreactive center of cryptochrome with ATP. Müller P, *et al.* Sci. Rep., 2014.

Highlights
2014

Radiobiology Toxicology

DNA repair Decorporation Decontamination
Nuclear medicine Nuclear energy Human toxicology
Individual radiosensitivity Alternative energies
Low doses Ecotoxicology
Nuclear energy Individual radiosensitivity
Bio-remediation DNA repair Bio-remediation
Ecotoxicology Human toxicology Low doses
Alternative energies Decontamination Decorporation

Science Translational Medicine

■ **Ultrahigh dose-rate FLASH irradiation increases the differential response between normal and tumor tissue in mice**

Favaudon V, Caplier L, Monceau V, Pouzoulet F, Sayarath M, Fouillade C, Poupon MF, Brito I, Hupe P, Bourhis J, Hall J, Fontaine JJ, Vozenin MC.

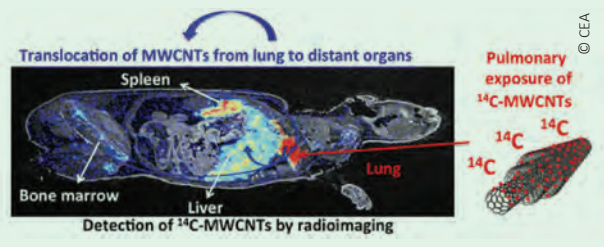
Sci. Transl. Med., 2014, 6 (245), 245ra93

ACS Nano

■ **Carbon Nanotube Translocation to Distant Organs after Pulmonary Exposure: Insights from in Situ C-14-Radiolabeling and Tissue Radioimaging**

Czarny B, Georgin D, Berthon F, Plastow G, Pinault M, Patriarche G, Thuleau A, L'Hermite MM, Taran F, Dive V.

ACS Nano, 2014, 8 (6), 5715-5724



Detection of carbon nanotube by radioimaging. Czarny B, *et al.* ACS Nano, 2014.

Mutation Research/Reviews in Mutation Research

■ **Crosstalk between telomere maintenance and radiation effects: A key player in the process of radiation-induced carcinogenesis**

Shim G, Ricoul M, Hempel WM, Azzam EI, Sabatier L.

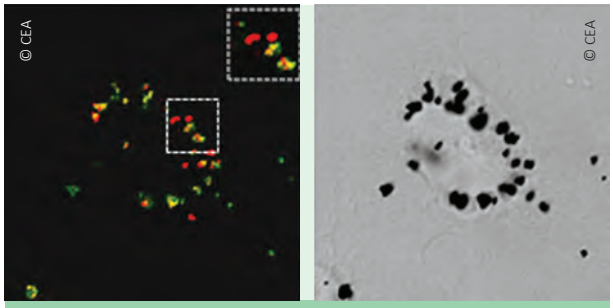
Mutat. Res.-Rev. Mutat. Res., 2014, 760, 1-17

Particle and Fibre Toxicology

■ **Low-solubility particles and a Trojan-horse type mechanism of toxicity: the case of cobalt oxide on human lung cells**

Ortega R, Bresson C, Darolles C, Gautier C, Roudeau S, Perrin L, Janin M, Floriani M, *et al.*

Part. Fibre Toxicol., 2014, 11: 14

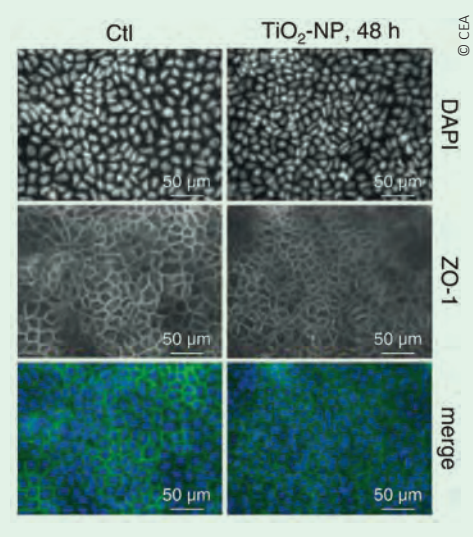


Confocal microscopy and TEM images of Co_3O_4 particles in human lung cells. Ortega R, *et al.* Part. Fibre Toxicol., 2014.

■ **Titanium dioxide nanoparticle impact and translocation through ex vivo, in vivo and in vitro gut epithelia**

Brun E, Barreau F, Veronesi G, Fayard B, Sorieul S, Chaneac C, Carapito C, Rabilloud T, *et al.*

Part. Fibre Toxicol., 2014, 11: 14



Integrity alteration of Caco-2 cells exposed to TiO_2-NPs vs non exposed (Ctl). Brun E, *et al.* Part. Fibre Toxicol. 2014.

Nanoscale

- **Analysis of cellular responses of macrophages to zinc ions and zinc oxide nanoparticles: a combined targeted and proteomic approach**

Triboulet S, Aude-Garcia C, Armand L, Gerdil A, Diemer H, Proamer F, Collin-Faure V, Habert A, *et al.*
Nanoscale, 2014, 6 (11), 6102-6114

- **Interference of CuO nanoparticles with metal homeostasis in hepatocytes under sub-toxic conditions**

Cuillel M, Chevallet M, Charbonnier P, Fauquant C, Pignot-Paintrand I, Arnaud J, Cassio D, Michaud-Soret I, Mintz E.
Nanoscale, 2014, 6 (3), 1707-1715

Cryobench at the Institute of Structural Biology, CEA/CNRS/Université J Fourier, Grenoble.

Preparing radio-labelled molecules. Biomedical Imaging Plateform Cyceron in Caen.

Highlights
2014

Diagnostic and therapeutic innovations

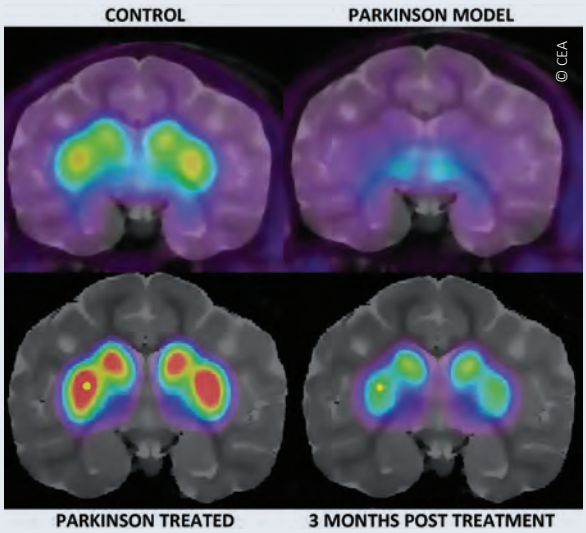
Biomarkers Biomedical imaging
Vaccines Neurologic and psychiatric diseases
Cancer Therapeutic targets Infectious diseases
Active molecules Translational research Immuno-analyses
Genetic diseases Cancer Disease models
Omics Infectious diseases Biomedical imaging Omics
Molecular labelling Bio-therapies Biomarkers
Genetic diseases Therapeutic targets Vaccines
Immuno-analyses Neurologic and psychiatric diseases
Bio-therapies Translational research Active molecules
Molecular labelling Disease models

Nature

■ **Neuropsychosocial profiles of current and future adolescent alcohol misusers**
Whelan R, Watts R, Orr CA, Althoff RR, Artiges E, Banaschewski T, Barker GJ, Bokde ALW, *et al.*
Nature, 2014, 512 (7513), 185-9

The Lancet

■ **Long-term safety and tolerability of ProSavin, a lentiviral vector-based gene therapy for Parkinson's disease: a dose escalation, open-label, phase 1/2 trial**
Palfi S, Gurruchaga JM, Ralph GS, Lepetit H, Lavisse S, Buttery PC, Watts C, Miskin J, *et al.*
Lancet, 2014, 383 (9923), 1138-1146



Prosavin induced dopamine secretion in NHP *in vivo*. Palfi S, *et al.* Lancet, 2014.

Nature Nanotechnologies

■ **Nature Nanotechnologies**
Gaudin A, Yemisci M, Eroglu H, Lepetre-Mouelhi S, Turkoglu OF, Donmez-Demir B, Caban S, Sargon MF, *et al.*
Nat. Nanotechnol., 2014, 9 (12), 1054-1062

Sickle-cell. Dussiot M, *et al.* Nat. Med., 2014.

Nature Genetics

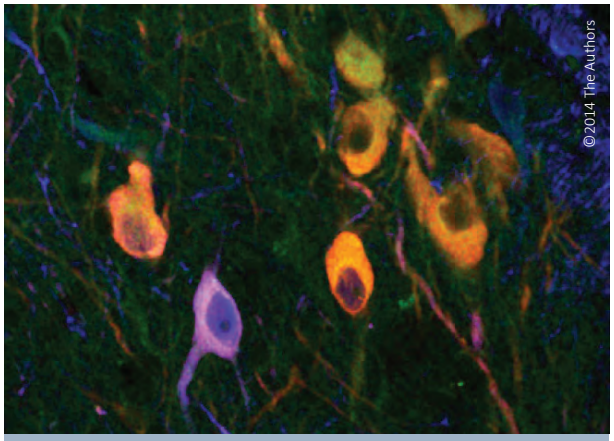
■ **Discovery of new risk loci for IgA nephropathy implicates genes involved in immunity against intestinal pathogens**
Kiryluk K, Li YF, Scolari F, Sanna-Cherchi S, Choi M, Verbitsky M, Fasel D, Lata S.
Nature Genet., 2014, 46 (11), 1187-1196

■ **Genome-wide association study identifies multiple susceptibility loci for diffuse large B cell lymphoma**
Cerhan JR, Berndt SI, Vijai J, Ghesquieres H, McKay J, Wang SS, Wang ZM, Yeager M, *et al.*
Nature Genet., 2014, 46 (11), 1233-1238

Nature Medicine

■ **An activin receptor IIA ligand trap corrects ineffective erythropoiesis in beta-thalassemia**
Dussiot M, Maciel TT, Fricot A, Chartier C, Negre O, Veiga J, Grapton D, Paubelle E, *et al.*
Nat. Med., 2014, 20 (4), 398-407

■ **Persistence and activation of malaria hypnozoites in long-term primary hepatocyte cultures**
Dembele L, Franetich JF, Lorthiois A, Gego A, Zeeman AM, Kocken CHM, Le Grand R, Dereuddre-Bosquet N, *et al.*
Nat. Med., 2014, 20 (3), 307-312



Human ESC-derived dopamine neurons. Grealish S, *et al.* Cell Stem Cell, 2014.

Cell Stem Cell

■ **Human ESC-Derived Dopamine Neurons Show Similar Preclinical Efficacy and Potency to Fetal Neurons when Grafted in a Rat Model of Parkinson's Disease**
Grealish S, Diguet E, Kirkeby A, Mattsson B, Heuer A, Bramoulle Y, Van Camp N, Perrier AL, Hantraye P, *et al.*
Cell Stem Cell, 2014, 15 (5), 653-665

The Lancet Neurology

■ **Pathogenesis of multiple sclerosis: insights from molecular and metabolic imaging**
Ciccarelli O, Barkhof F, Bodini B, De Stefano N, Golay X, Nicolay K, Pelletier D, Pouwels PJW, *et al.*
Lancet Neurol., 2014, 13 (8), 807-822

Trends in Cognitive Sciences

■ **Characterizing the dynamics of mental representations: the temporal generalization method**
King JR, Dehaene S.
Trends Cogn. Sci., 2014, 18 (4), 203-210

Journal of Clinical Oncology

■ **Loss of Major Molecular Response as a Trigger for Restarting Tyrosine Kinase Inhibitor Therapy in Patients With Chronic-Phase Chronic Myelogenous Leukemia Who Have Stopped Imatinib After Durable Undetectable Disease**
Rousselot P, Charbonnier A, Cony-Makhoul P, Agape P, Nicolini FE, Varet B, Gardembas M, Etienne G, *et al.*
J. Clin. Oncol., 2014, 32 (5), 424-30

Journal of the National Cancer Institute

■ **The Effect on Melanoma Risk of Genes Previously Associated With Telomere Length**
Iles MM, Bishop DT, Taylor JC, Hayward NK, Brossard M, Cust AE, Dunning AM, Lee JE, *et al.*
J. Natl. Cancer Inst., 2014, 106 (10), 5135

Molecular Psychiatry

■ **A genome-wide association meta-analysis of plasma A beta peptides concentrations in the elderly**
Chouraki V, de Bruijn RFAG, Chapuis J, Bis JC, Reitz C, Schraen S, Ibrahim-Verbaas CA, Grenier-Boley B, *et al.*
Mol. Psychiatr., 2014, 19 (12), 1326-1335

■ **White-matter microstructure and gray-matter volumes in adolescents with subthreshold bipolar symptoms**
Paillère-Martinot ML, Lemaitre H, Artiges E, Miranda R, Goodman R, Penttila J, Struve M, Fadai T, *et al.*
Mol. Psychiatr., 2014, 19 (4), 462-470

Following the fibers: MRI brain imaging at the Institute of Biomedical Imaging in Orsay.

Gastroenterology

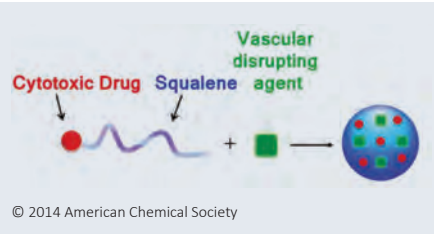
■ **Patients With Colorectal Tumors With Microsatellite Instability and Large Deletions in HSP110 T-17 Have Improved Response to 5-Fluorouracil-Based Chemotherapy**
Collura A, Lagrange A, Svrcek M, Marisa L, Buhard O, Guilloux A, Wanherdrick K, Dorard C, *et al.*
Gastroenterology, 2014, 146 (2), 401-411

The American Journal of Psychiatry

■ **Neural and Cognitive Correlates of the Common and Specific Variance Across Externalizing Problems in Young Adolescence**
Castellanos-Ryan N, Struve M, Whelan R, Banaschewski T, Barker GJ, Bokde ALW, Bromberg U, Buchel C, *et al.*
Am. J. Psychiat., 2014, 171 (12), 1310-1319

ACS Nano

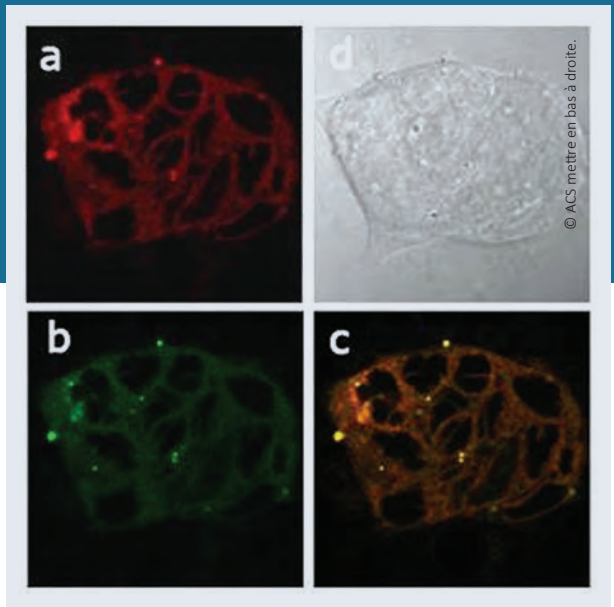
■ **Therapeutic Modalities of Squalenoyl Nanocomposites in Colon Cancer: An Ongoing Search for Improved Efficacy**
Maksimenko A, Alami M, Zouhiri F, Brion JD, Pruvost A, Mougin J, Hamze A, Boissenot T, *et al.*
ACS Nano, 2014, 8 (3), 2018-2032



Strategy to achieve well-defined nanoassemblies for multidrug therapy. Maksimenko A, *et al.* ACS Nano, 2014.

PLOS Biology

■ **Haploinsufficiency of Dmxl2, Encoding a Synaptic Protein, Causes Infertility Associated with a Loss of GnRH Neurons in Mouse**
Tata B, Huijbregts L, Jacquier S, Csaba Z, Genin E, Meyer V, Leka S, Dupont J, *et al.*
PLoS. Biol., 2014, 12 (9), e1001952



Cell internalization of the squalene-based nanocomposites. Maksimenko A, *et al.* ACS Nano, 2014.

Autophagy

■ **New horizons in schizophrenia treatment: autophagy protection is coupled with behavioral improvements in a mouse model of schizophrenia**
Merenlender-Wagner A, Shemer Z, Touloumi O, Lagoudaki R, Giladi E, Andrieux A, Grigoriadis NC, Gozes I.
Autophagy, 2014, 10 (12), 2324-2332

Angewandte Chemie International Edition

■ **A Diiron(III,IV) Imido Species Very Active in Nitrene-Transfer Reactions**
Goure E, Avenier F, Dubourdeaux P, Seneque O, Albrieux F, Lebrun C, Clemancey M, Maldivi P, Latour JM.
Angew. Chem.-Int. Edit., 2014, 53 (6), 1580-1584

■ **Copper-Chelating Azides for Efficient Click Conjugation Reactions in Complex Media**
Bevilacqua V, King M, Chaumontet M, Nothisen M, Gabillet S, Buisson D, Puente C, Wagner A, Taran F.
Angew. Chem.-Int. Edit., 2014, 53 (23), 5872-5876

■ **Highly Reactive Nonheme Iron(III) Iodosylarene Complexes in Alkane Hydroxylation and Sulfoxidation Reactions**
Hong S, Wang B, Seo MS, Lee YM, Kim MJ, Kim HR, Ogura T, Garcia-Serres R, Clemancey M, Latour JM, Nam W.
Angew. Chem.-Int. Edit., 2014, 53 (25), 6388-6392

Journal of Allergy and Clinical Immunology

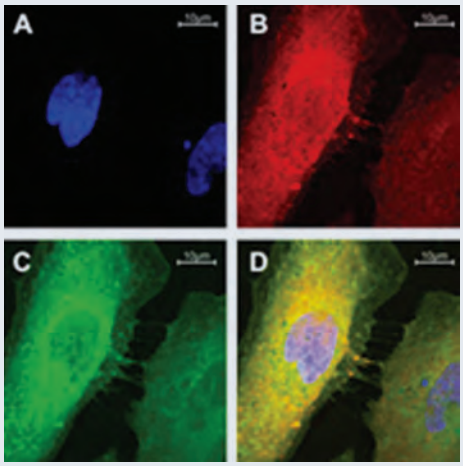
■ **Increased regulatory T-cell numbers are associated with farm milk exposure and lower atopic sensitization and asthma in childhood**
Lluis A, Depner M, Gaugler B, Saas P, Casaca VI, Raedler D, Michel S, Tost J, *et al.*
J. Allergy Clin. Immunol., 2014, 133 (2), 551-9

The American Journal of Human Genetics

■ **ELOVLS Mutations Cause Spinocerebellar Ataxia 38**
Di Gregorio E, Borroni B, Giorgio E, Lacerenza D, Ferrero M, Lo Buono N, Ragusa N, Mancini C, *et al.*
Am. J. Hum. Genet., 2014, 95 (2), 209-217

■ **Loss of Association of REEP2 with Membranes Leads to Hereditary Spastic Paraplegia**
Esteves T, Durr A, Mundwiller E, Loureiro JL, Boutry M, Gonzalez MA, Gauthier J, El-Hachimi KH, *et al.*
Am. J. Hum. Genet., 2014, 94 (2), 268-277

■ **Mutations in QARS, Encoding Glutaminyl-tRNA Synthetase, Cause Progressive Microcephaly, Cerebral-Cerebellar Atrophy, and Intractable Seizures**
Zhang XC, Ling JQ, Barcia G, Jing LL, Wu J, Barry BJ, Mochida GH, Hill RS, *et al.*
Am. J. Hum. Genet., 2014, 94 (4), 547-558



Confocal microscopy of cells after treatment to confirm localization of the click conjugate. Bevilacqua V *et al.*, Angew. Chem.-Int. Edit., 2014.

Cell, virus and bacteria analysis at the center for Infectious Diseases Models and Innovative Therapies in Fontenay-aux-Roses.

Nature Communications

■ **Variation in genomic landscape of clear cell renal cell carcinoma across Europe**
Scelo G, Riazalhosseini Y, Greger L, Letourneau L, Gonzalez-Porta M, Wozniak MB, Bourgey M, Harnden P, *et al.*
Nat. Commun., 2014, 5, 5135

Genome Biology

■ **Comparative analyses of Legionella species identifies genetic features of strains causing Legionnaires' disease**
Gomez-Valero L, Rusniok C, Rolando M, Neou M, Dervins-Ravault D, Demirtas J, Rouy Z, Moore RJ, *et al.*
Genome Biol., 2014, 15 (11), 505

■ **Genome-wide DNA methylation profiles in progression to in situ and invasive carcinoma of the breast with impact on gene transcription and prognosis**
Fleischer T, Frigessi A, Johnson KC, Edvardsen H, Touleimat N, Klajic J, Riis MLH, Haakensen VD, *et al.*
Genome Biol., 2014, 15 (8), 435

Advanced Functional Materials

■ **Nanometric Micelles with Photo-Triggered Cytotoxicity**
Anilkumar P, Gravel E, Theodorou I, Gombert K, Theze B, Duconge F, Doris E.
Adv. Funct. Mater., 2014, 24 (33), 5246-5252

Super-resolution microscopy in the Institute of Structural Biology, CEA/CNRS/Université Joseph Fourier, Grenoble.

Brain

■ **Large scale screening of neural signatures of consciousness in patients in a vegetative or minimally conscious state**
Sitt JD, King JR, El Karoui I, Rohaut B, Faugeras F, Gramfort A, Cohen L, Sigman M, Dehaene S, Naccache L.
Brain, 2014, 137, 2258-2270

■ **The wide spectrum of tubulinopathies: what are the key features for the diagnosis?**
Bahi-Buisson N, Poirier K, Fourniol F, Saillour Y, Valence S, Lebrun N, Hully M, Bianco CF, *et al.*
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■ **The role of microglia in human disease: therapeutic tool or target?**
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Highlights
2014

Molecular and cellular mechanisms of living organisms

Normal and pathological mechanisms
Human genomic High-throughput screening
Integrated structural biology Genome biology
Large-scale biology Normal and pathological mechanisms
Human genomic Integrated structural biology
High-throughput screening Genome biology
Large-scale biology

Highlights 2014

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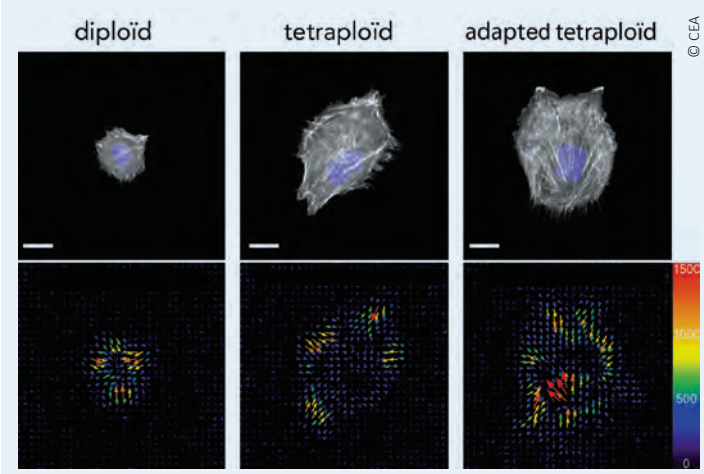

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Evolutionary mechanisms demonstrated for an architect gene. From algae (blue) to foam (green) then flowers (red /orange). Sayou C, *et al.* Science, 2014.

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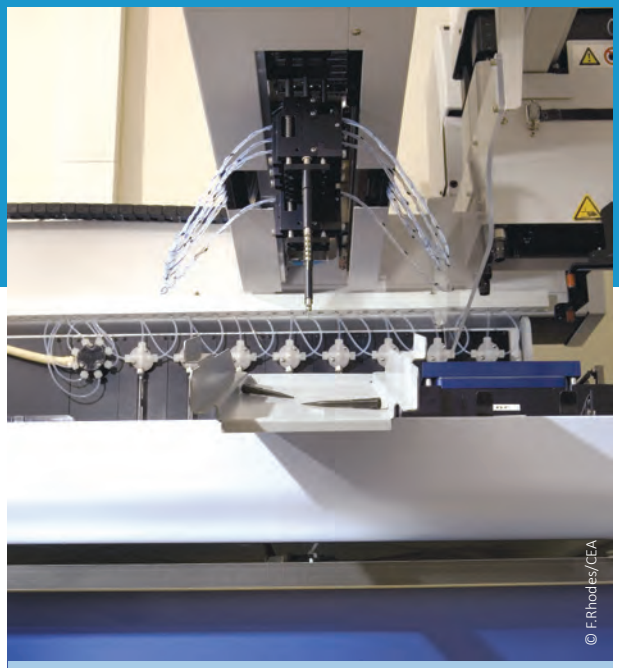

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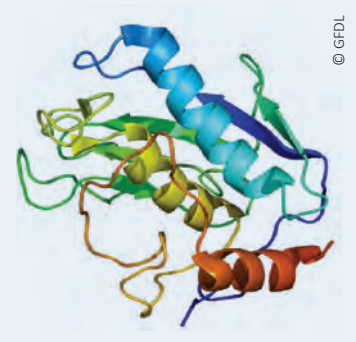
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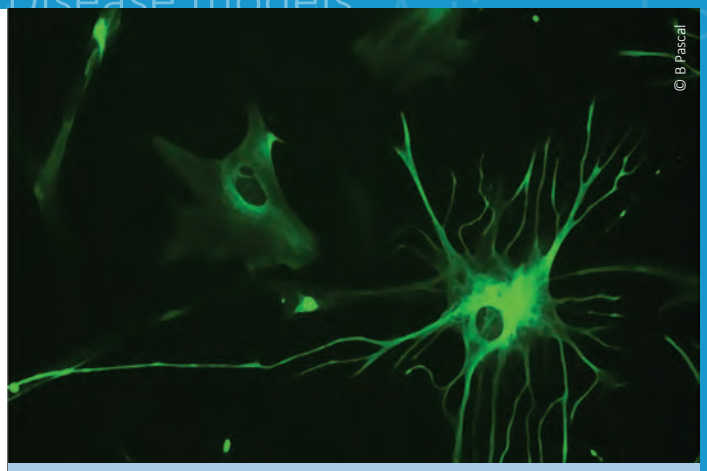
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Crystal structure of Nipah virus unassembled nucleoprotein (blue) in complex with its viral chaperone (red). Yabukarski *et al.*, Nat. Struct. Mol. Biol., 2014.

■ **The Crystal Structure of Fe4S4 Quinolinate Synthase Unravels an Enzymatic Dehydration Mechanism That Uses Tyrosine and a Hydrolase-Type Triad**
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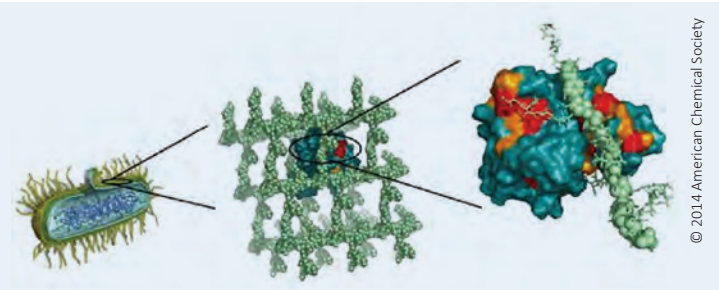

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■ **Crystal Structure of Tryptophan Lyase (NosL): Evidence for Radical Formation at the Amino Group of Tryptophan**
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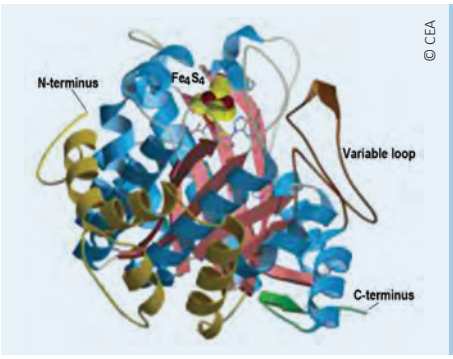

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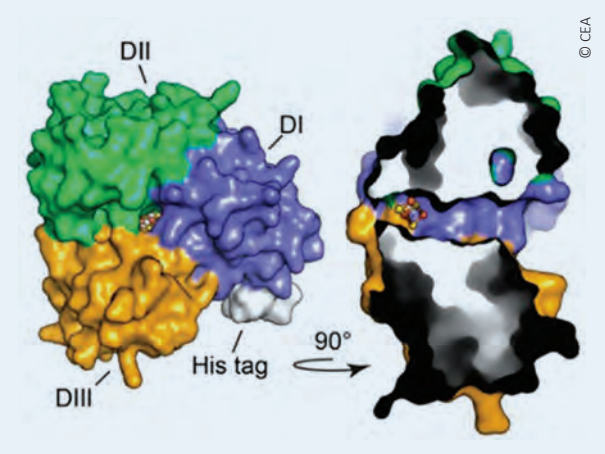

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■ **Formation of High-Valent Iron-Oxo Species in Superoxide Reductase: Characterization by Resonance Raman Spectroscopy**
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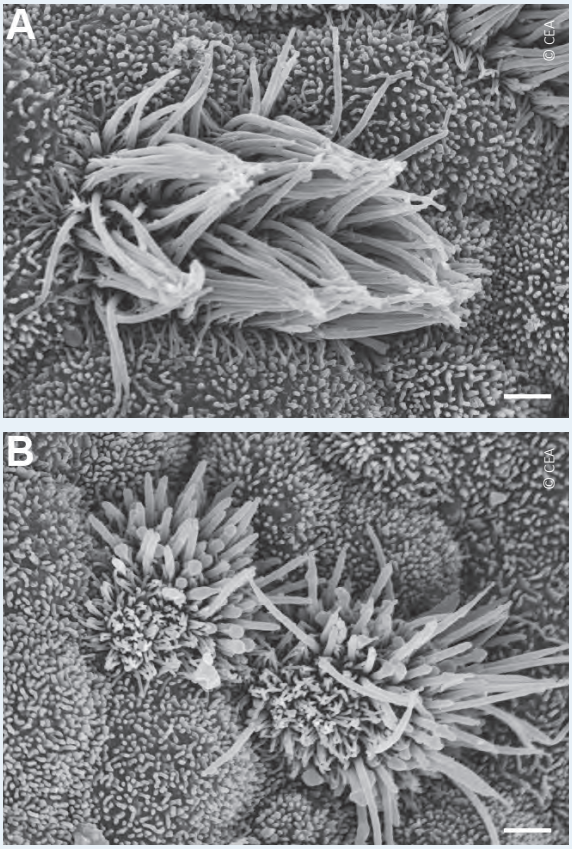

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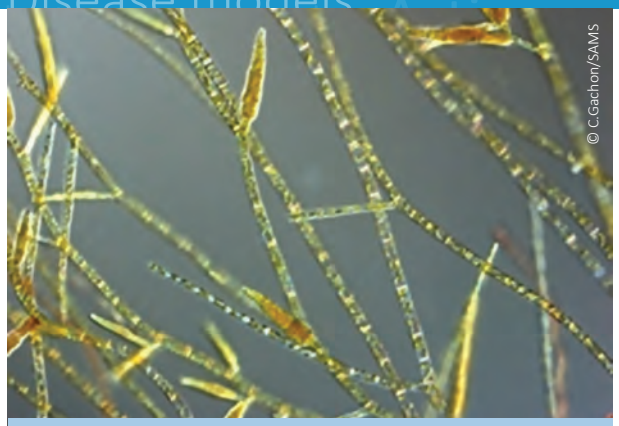

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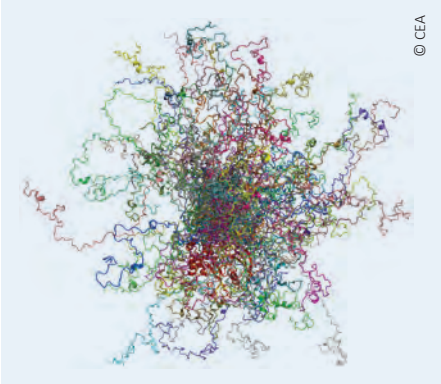

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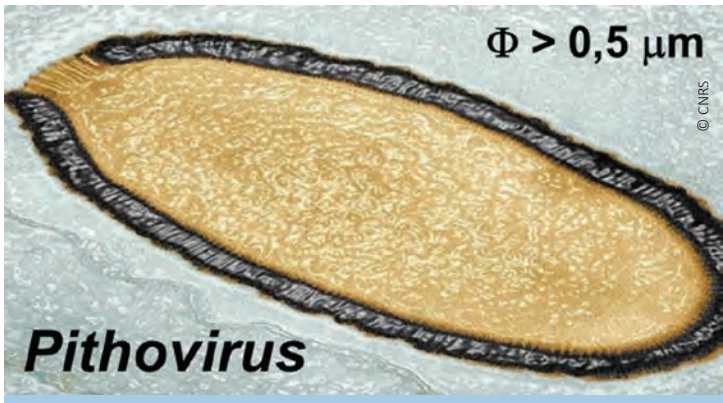

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Technological developments

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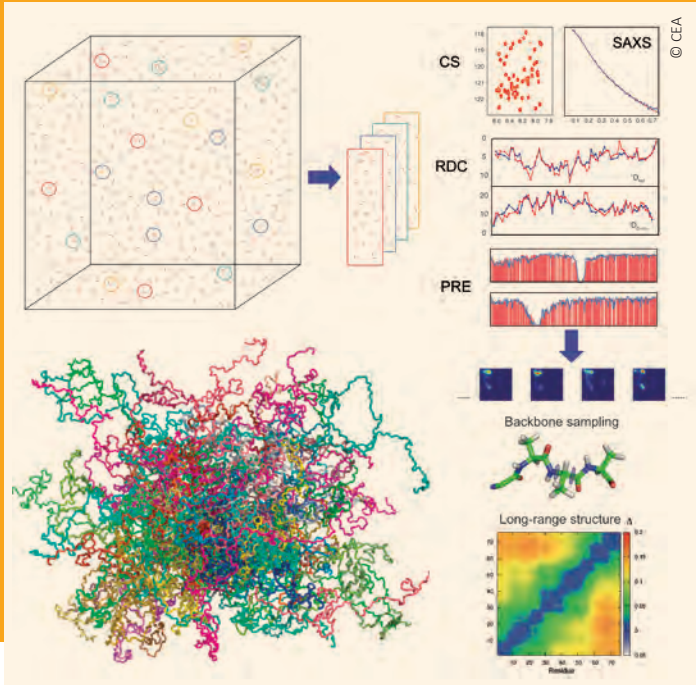

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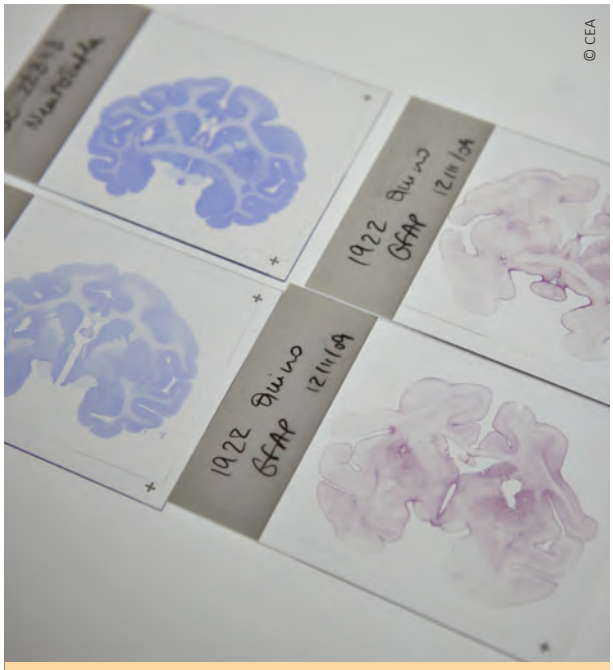

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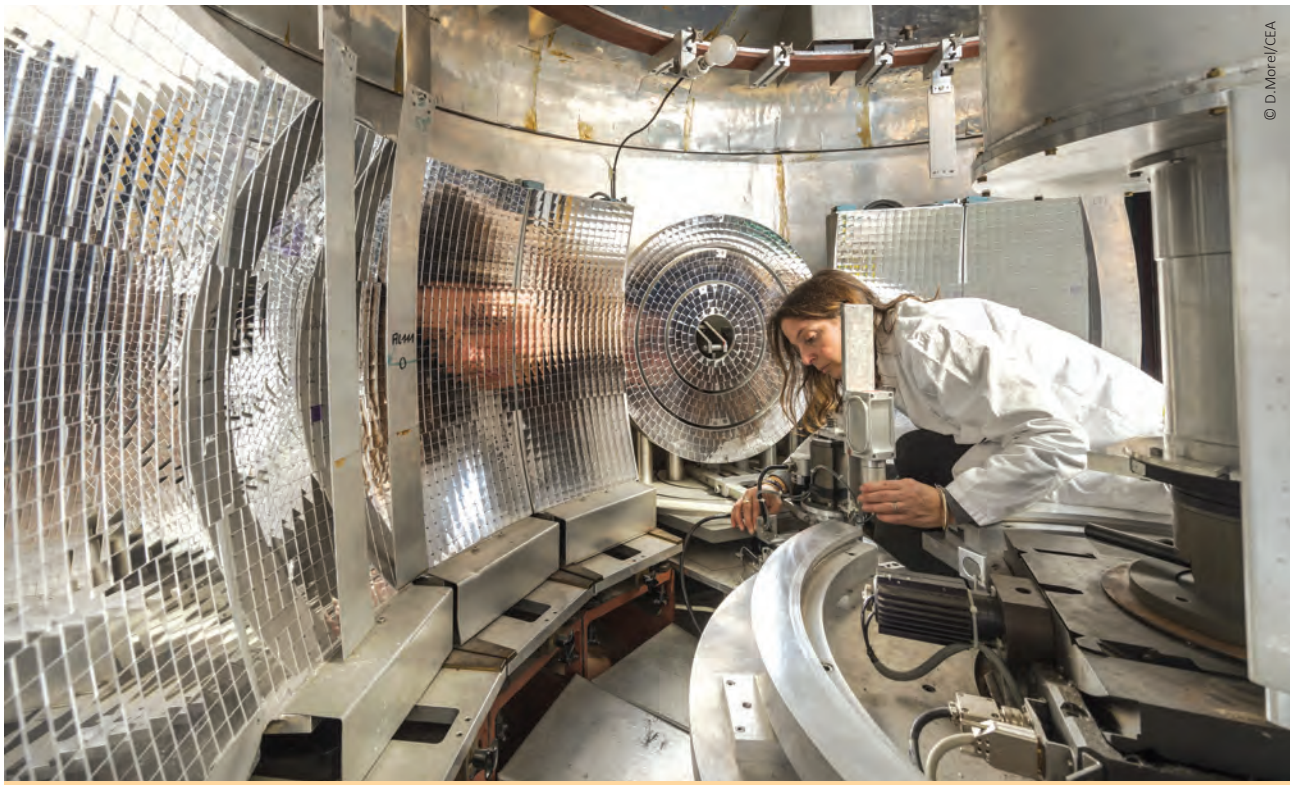

Implementation of an experiment in the high-flux reactor of the Laue Langevin Institute in Grenoble.

CEA Life Sciences Division
Direction des Sciences du vivant
18, route du Panorama, BP6
F92265 Fontenay-aux-Roses
dsv@cea.fr
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