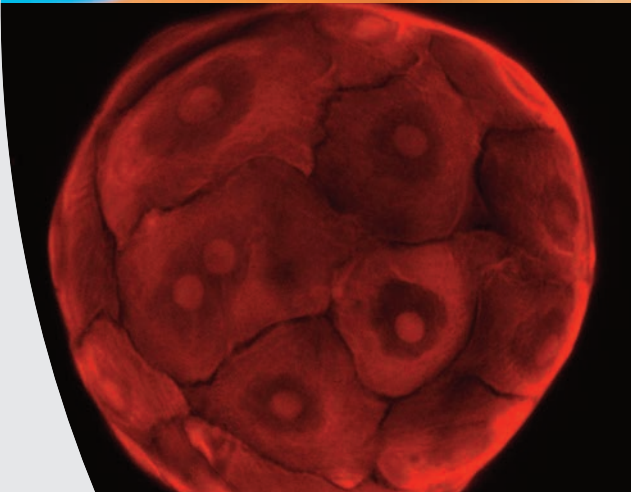




INSTITUT DE FRANCE  
Académie des sciences



## Exposés scientifiques d'associés étrangers élus à l'Académie des sciences en 2015

*séance en anglais*

Mardi 26 septembre 2017 de 14h30 à 16h30  
en grande salle des séances

23, quai de Conti, 75006 Paris

### P programme

Sébastien CANDEL, Président de l'Académie des sciences

Catherine BRÉCHIGNAC, Secrétaire perpétuel de l'Académie des sciences

Pascale COSSART, Secrétaire perpétuel de l'Académie des sciences

**14:30** Présentation de Max Cooper par Jean-Claude Weill  
membre de l'Académie des sciences, Professeur d'Immunologie  
à INEM - Institut Necker-Enfants Malades - INSERM, France

#### Evolution of an adaptive immune system

Max COOPER, professeur à l'université d'Emory, États-Unis  
élu dans la section de biologie humaine et sciences médicales

**15:00** Présentation de Hans Clevers par Daniel Louvard  
membre de l'Académie des sciences, professeur honoraire à  
l'Institut Pasteur et directeur honoraire de l'Institut Curie, France

#### Lgr5 Stem Cell-based organoids in human disease

Hans CLEVERS, professeur à l'Institut Hubrecht, Pays-Bas  
élu dans la section de biologie moléculaire et cellulaire, génomique

**15:30** Présentation de Sandra Diaz par Jean-Dominique Lebreton  
membre de l'Académie des sciences, France

#### Searching for general patterns of plant functional diversity

Sandra DIAZ, professeur à l'université nationale de Cordoba,  
Argentine  
élu(e) dans la section de biologie intégrative

**16:00** Discussion générale et conclusion

Dès sa création en 1666 l'Académie des sciences témoigne de son ouverture sur le monde par l'élection de membres associés étrangers. Choisis parmi les savants étrangers les plus éminents, ils contribuent aux travaux et à la réputation internationale de l'Académie. Ainsi, de nombreux grands noms qui ont marqué l'histoire scientifique de leur discipline ont intégré la compagnie tels que : Charles Darwin, Albert Einstein, Alexander Flemming, Benjamin Franklin, Alexander von Humboldt, Christian Huygens, Robert Koch, Isaac Newton, Alessandro Volta... C'est en perpétuant cette tradition qu'au terme des élections ouvertes en 2015, l'Académie des sciences a élu 15 nouveaux associés étrangers parmi lesquels figurent Max Cooper, Hans Clevers et Sandra Diaz. Cette séance sera l'occasion pour ces derniers de présenter respectivement leurs travaux en immunologie, biologie cellulaire et écologie des écosystèmes pour lesquels ils ont été élus à l'Académie.

## Biographies et résumés



### Max COOPER

Professeur à l'université d'Emory, États-Unis

Drawing on the examination of children with genetic deficiencies, Max Cooper demonstrated the existence of deficiencies affecting either humoral immunity or cellular immunity. This demonstration, led him to forge the notion that two independent cell lines accounted for these two types of immunity. This major discovery would shortly be followed by Max Cooper's discovery of B lymphocytes – the agents of humoral immunity. Based on these findings, he then conceived a model describing the early stages of human lymphocyte development and the steps leading to malignant transformations. In recent years, Max Cooper's work has been focusing on the study of the mechanisms that contributed to the evolution of the immune system, as represented in mammals, using the Lamprey as a model.

### Evolution of an adaptive immune system

Recent phylogenetic studies indicate that T cells and B cells have been constant companions in vertebrates for more than 500 million years. For antigen recognition, however, the lymphocytes in the extant jawless vertebrate representatives, lampreys and hagfish, use variable lymphocyte receptors that are composed of leucine-rich-repeat sequences instead of immunoglobulin V(D)J and C domains. Convergent evolution may account for these alternative solutions to achieve specific adaptive immunity. Characterization of monoclonal lamprey antibodies indicate that they are as antigen-specific as mouse and human antibodies and can recognize unique antigens, including novel target epitopes on human tumor cells.



## Hans CLEVERS

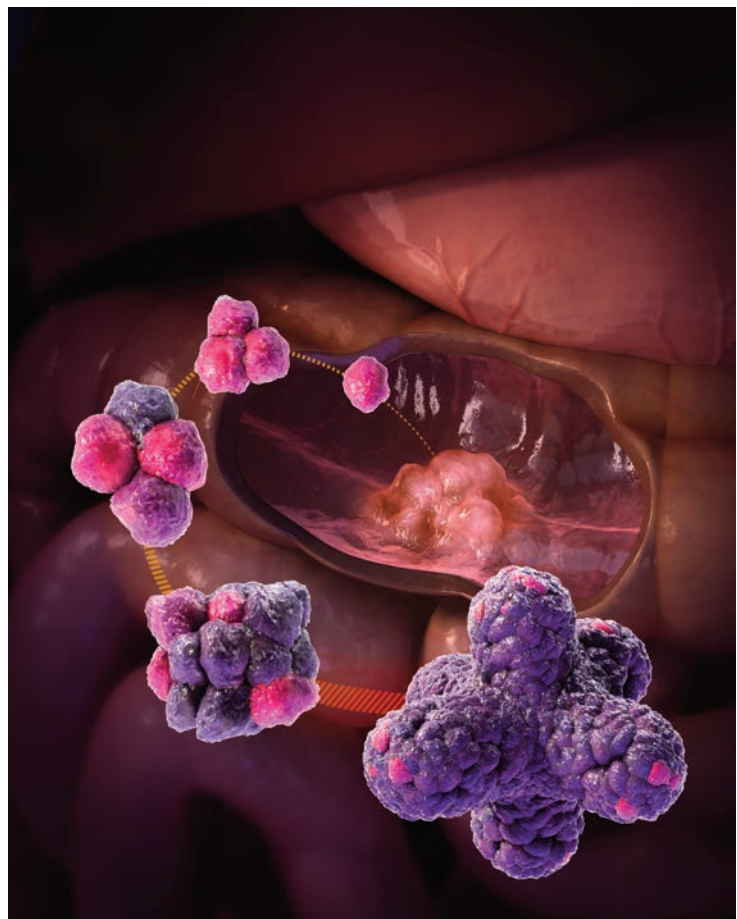
Professeur à l'Institut Hubrecht, Pays-Bas

Hans Clevers' work has profoundly influenced our understanding of the biology of the intestine and of stem cells in general. He has been playing a pioneering role in establishing conceptual links between adult stem cell differentiation and carcinogenesis at the molecular level. He has in particular identified Lgr5 as the target of the Wnt-TCF4 pathway and as the marker of stem cells of the intestine and of other tissues. He has recently shown how to use the R spondin/Lgr5 interactions to generate long term clonal cultures. Finally, he has largely contributed to develop organoids which have become useful models that mimic different organs such as the intestine, liver and, more recently, pancreas. He was awarded the Breakthrough Prize in Life Sciences in 2013.

### Lgr5 Stem Cell-based organoids in human disease

The intestinal epithelium is the most rapidly self-renewing tissue in adult mammals. We originally defined Lgr5 as a Wnt target gene, transcribed in colon cancer cells. Two knock-in alleles revealed exclusive expression of Lgr5 in cycling, columnar cells at the crypt base. Using lineage tracing experiments in adult mice, we found that these Lgr5+ve crypt base columnar cells (CBC) generated all epithelial lineages throughout life, implying that they represent the stem cell of the small intestine and colon. Lgr5 was subsequently found to represent an exquisitely specific and almost 'generic' marker for stem cells, including in hair follicles, kidney, liver, mammary gland, inner ear tongue and stomach epithelium.

Single sorted Lgr5+ve stem cells can initiate ever-expanding crypt-villus organoids, or so called 'mini-guts' in 3D culture. The technology is based on the observation that Lgr5 is the receptor for a potent stem cell growth factor, R-spondin. Similar 3D cultures systems have been developed for the Lgr5+ve stem cells of human stomach, liver, pancreas, prostate and kidney. Using CRISPR/Cas9 technology, genes can be efficiently modified in organoids of various origins.





## Sandra DIAZ

Professeur à l'université nationale de Cordoba, Argentine  
Sandra Diaz is a main figure of community and ecosystems ecology, the branch of ecology that studies assemblages of species, and how they affect the flows of matter and energy in the world. She has made fundamental contributions to the development of the theory and practical methods of functional diversity, or the ways in which the phenotypic characteristics of organisms affect, and are affected by, the environment. The relevance of Sandra Diaz's work for such major topical issues as the interactions between global environmental change and biodiversity, and the consequences of these for human wellbeing, has led her to take a prominent role in major international programs

### Searching for general patterns of plant functional diversity

The remarkable variety of plant form and function is cherished around the world. At the same time, if we are to understand and manage biodiversity and ecosystems, general patterns underlying this diversity need to be identified. By analysing worldwide variation in major traits critical to growth, survival and reproduction within the largest sample of vascular plant species ever compiled, we provide the first quantitative picture of essential functional diversity of vascular plants on Earth. We found that the trait space occupied by extant plants is strongly constrained and can be captured by a two-dimensional global spectrum of plant form and function. One major dimension within this plane reflects the size of whole plants and their parts; the other represents balances leaf construction costs against growth potential. Our findings establish a backdrop onto which to map plant lineages, evolutionary trajectories, and historical and contemporary plant communities in the face of past and ongoing environmental change.

