Adrian Constantin Apetri, PhD

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EDUCATION

Postdoctoral Associate, Howard Hughes Medical Institute, YALE University, CT, USA 2006- 2009

Postdoctoral Associate, Case Western Reserve University, Cleveland, OH, USA 2004- 2005

Ph.D., Protein Biochemistry, Case Western Reserve University, Cleveland, Ohio, USA 1999-2004

M.Sc., Organic Chemistry, Babes-Bolyai University, Cluj-Napoca, Romania 1991-1997

WORK

Scientific Director, Biophysics and Process Analytics- Janssen Vaccines and Prevention 2020-

- Leading a multidisciplinary team focused on vaccine process development analytics and biophysics
- Automation and robotics PAT implementation
- Real Time analytics for vaccine development processes
- Early analytical development of protein, RNA and adeno vector-based vaccines

Scientific Director, Janssen Prevention Center, Leiden, NL 2015-2019

- Led a multidisciplinary team focused on antibody discovery, affinity and functionality optimization, structural biology, biophysics, protein analytics and mass spectrometry, assay development, biomarker discovery, *ex vivo* and *in vivo* POC studies in the field of Alzheimer's and related neurodegenerative diseases
- Leading and scientific coordination of the Alzheimer Discovery program in collaboration with multiple academic and industrial partners

Sr. Scientist, Head Antibody and Protein Analytics, Crucell Vaccine Institute, Leiden, NL 2009-2014

- Led team of scientists focused on extensive analytical and biophysical characterization of antibodies (IgG, single domains, multi domains, bi-functional) and other protein drug and vaccine candidates (gp140, mini HA Influenza vaccine) and their transfer towards development; pre-formulation and stability
- Full range of de-risking and protein developability studies for smooth transition towards NME declarations

SCIENTIFIC PUBLICATIONS

- Marreiro A, Van Kolen K, Sousa C, Temmerman L, Vasconcelos B, Crespo-Rodriguez R, van Weering JRT, Van Dam D, De Deyn PP, **Apetri A**, Schoofs L, Mercken MH. "*Comparison of size distribution and (Pro249-Ser258) epitope exposure in in vitro and in vivo derived Tau fibrils",* (2020) *BMC Mol Cell Biol* **21**(1), 81-86

- Puchades C, Kükrer B., Sneekes-Vriese E., Diefenbach O. and **Apetri A.** *"*Semi high-throughput epitope mapping of influenza Hemagglutinin drug candidates using HDX-MS"*,* (2019) *Sci Rep.* **18** 4735-40

- Li X., Koudstaal W., Fletcher L., Costa M., van Winsen M., Siregar B., Inganäs B., Kim J., Keogh E., Macedo J., Holland T., Perry S., Bard F., Hoozemans JJ., Goudsmit J., **Apetri A**, Pascual G., "Naturally-occurring antibodies isolated from PD patients inhibit synuclein seeding *in vitro* and recognize Lewy pathology", (2019) *Acta Neuropathol*. **137**(5), 825-836

- **Apetri A**., Crespo R., Juraszek J., Pascual G., Janson R., Keogh E., Holland T., Wadia J., Verveen H., Siregar B., Taggenbrock R., van Ameijde J., van Winsen M., Inganäs H., Koldijk M., Stoop E., Zuijdgeest D., de Marco D., Borgers M., Dockx K, Zhu X., Mrosek M., Steinbacher S., Ummenthum K., Hoozemans J., Wilson IA., Koudstaal W. and Goudsmit J. "Common antigenic motif recognized by naturally occurring human Vh5-51/Vl4-1 anti tau antibodies with distinct functionality" (2018) *Acta Neuropathol. Comm*. **6** (1): 43

- Van Ameijde J., Crespo R., Janson R., Juraszek J., Siregar B., Verveen H, Sprengers I., Nahar T., Hoozemans JJ., Steinbacher S., Willems R., Delbroek L., Borgers M., Dockx K., Van Kolen K., Mercken M., Pascual G., Koudstaal W., and **Apetri A.** "Enhancement of therapeutic potential of a naturally occurring human antibody targeting a phosphorylated Ser^{422} containing epitope on pathological tau" (2018) *Acta Neuropathol. Comm*. **6** (1): 59

- De Marco D., Taggenbrock R., Crespo R., Koudstaal W, Ramsburg E., and **Apetri A.** "A cell-based assay to study antibody-mediated tau clearance by microglia" J Vis Exp. (2018) **141**

- Zhang H., Zhu X., Pascual G., Wadia JS., Keogh E., Hoozemans JJ., Siregar B., Inganäs H., Stoop EJM., Goudsmit J., **Apetri A**., Koudstaal W., and Wilson IA. "Structural Basis for Recognition of a Novel Epitope by a Human Anti-tau Antibody" *Structure* (2018) **26** (12), 1626-1634

- Crespo R., Koudstaal W. and **Apetri A**. "*In vitro* assay for studying the aggregation of tau protein and drug screening" (2018) J Vis Exp. **20** (141)

- Pascual G., Wadia JS., Zhu X., Keogh E., Kükrer B., van Ameijde J., Inganäs H., Siregar B., Perdok G., Diefenbach O., Nahar T., Sprengers I., Koldijk MH., Brinkman van der Linden EC., Peferoen LA., Zhang H., Yu W, Li X., Wagner M., Moreno V., Kim J., Costa M., West K., Fulton Z., Chammas L., Luckashenak N., Fletcher L., Holland T., Arnold C., Williamson AR., Hoozemans JJ., **Apetri A.**, Bard F., Wilson IA., Koudstaal W., Goudsmit J. "Immunological memory to hyperphosphorylated tau in asymptomatic individuals" (2017) *Acta Neuropathol.* **133** (5):767-783

- Impagliazzo A., Milder F., Kuipers H., Wagner MV., Zhu X., Hoffman RM., van Meersbergen R., Huizingh J., Wanningen P., Verspuij J., de Man M., Ding Z., **Apetri A.**, Kükrer B., Sneekes-Vriese E., Tomkiewicz D., Laursen NS., Lee PS., Zakrzewska A., Dekking L., Tolboom J., Tettero L., van Meerten S., Yu W., Koudstaal W., Goudsmit J., Ward AB., Meijberg W., Wilson IA., Radošević K., "A stable trimeric influenza hemagglutinin stem as a broadly protective immunogen" (2015) *Science* **349** (6254):1301-6.

- Nkolola JP, Bricault CA, Cheung A, Shields J, Perry J, Kovacs JM, Giorgi E, van Winsen M, **Apetri A**, Brinkman-van der Linden EC, Chen B, Korber B, Seaman MS, Barouch DH. "Characterization and Immunogenicity of a Novel Mosaic M HIV1 gp140 trimer (2014) *J. Virol.* **88** (17):9538-52

- Horwich AL., **Apetri AC.** and Fenton WA. "The GroEL/GroES cis cavity as a passive anti-aggregation device" (2009) *FEBS Lett.* **583** (16):2654-62

- **Apetri AC.** and Horwich AL. "Chaperonin chamber accelerates protein folding through passive action of preventing aggregation" (2008) *Proc. Natl. Acad. Sci.* **105** (45):17351-5

- Cobb NJ., **Apetri AC.** and Surewicz WK. "Prion protein amyloid formation under native-like conditions involves refolding of the C-terminal α-helical domain" (2008) *J. Biol. Chem.,* **283**, 34704 – 34711

- **Apetri AC.**, Maki K., Roder H. and Surewicz WK. "Early Intermediate in Human Prion Protein Folding as Evidenced by Ultrarapid Mixing Experiments" (2006) *J. Am. Chem. Soc* **128** (35), 11673-8

- Surewicz WK., Jones EM., **Apetri AC.** "The Emerging Principles of Mammalian Prion Propagation and Transmissibility Barriers: Insight from Studies in Vitro" (2006) *Acc. Chem. Res.* **39** (9), 654-62

- **Apetri AC**., Vanik DL. and Surewicz WK. "Polymorphism at Residue 129 Modulates the Conformational Conversion of the D178N Variant of Human Prion Protein 90-231" (2005) *Biochemistry* **44** (48), 15880-15888

- **Apetri AC**., Surewicz K and Surewicz WK. "The Effect of Disease-associated Mutations on the Folding Pathway of Human Prion Protein" (2004) *J. Biol. Chem.* **279,** 18008-14

- **Apetri AC**. and Surewicz WK. "Atypical Effect of Salts on the Thermodynamic Stability of Human Prion Protein" (2003) *J. Biol. Chem.* **278**, 22187-92

- **Apetri AC**. and Surewicz WK. "Kinetic Intermediate in the Folding of Human Prion Protein" (accelerated publication) (2002) *J. Biol. Chem.* **277**, 44589-92

- Baldea I, Panea I and **Apetri AC**. "Polymethine dyes. Part II. The photochromic behavior of some cationic dimethine dyes" (1999) *STUDIA UNIVERSITATIS, CHEMIA* **44**(1-2), 117-125

PATENTS

- *Human binding molecules capable of binding to and neutralizing hepatitis b viruses and uses thereof*
  Den Nieuwenhof Ingrid Van, Der Neut Kolfschoten Marijn Van, Constantin Adrian Apetri, and Robert Heinz Edward Friesen
  WO 2014048910 A1

- *Improved Anti-Human Tau HVPGGGSVQIVYKPVDLSKV antibody*
  Jaroslav Juraszek and Adrian Apetri
  Patent application number: 17163425.6-1412

- *Methods for detection of Tau protein aggregation modulating compounds*
  Rosa Crespo and Adrian Apetri
  WO EP US CN ~~JP~~ ~~KR~~ AU CA EA SG CA3055866A1

- *Binding molecules that specifically bind to Tau*
  Hanneke Verveen, Berdien Siregar, Roosmarijn Janson, Jaroslav Juraszek, and Adrian Apetri
  WO EP US CN JP KR AU CA EA SG CA3056517A1

- *Anti Synuclein antibodies*
  Gabriel Pascual, Constantin Adrian Apetri and Xinji LI
  WO *EP US CN JP* KR *AU ~~BR~~ CA* EA MX *CA3111907A1*

TECHNICAL EXPERTISE

Biophysical techniques:

Spectroscopy (UV-VIS, Circular dichroism, Fourier Transformed Infra-Red, Raman), Multi-Angle and Dynamic Light scattering, Capillary Electrophoresis, Size Exclusion Chromatography, Asymmetric Flow Field Flow Fractionation, Differential Scanning Calorimetry, Isothermal Titration Calorimetry, Stopped flow and continuous flow techniques, Fluorescence (intrinsic, resonance energy transfer, anisotropy), Mass Spectrometry (Intact mass, peptide mapping, glycan analysis), epitope mapping and conformational dynamics by Hydrogen-Deuterium Exchange Mass Spectrometry, Atomic Force Microscopy.

Protein purification and analysis

Protein expression in mammalian (multiple formats) and bacterial cells, Affinity, Ion exchange, Hydrophobic interaction, Size exclusion, Normal phase and Reversed phase chromatography; SDS-page, IEF, western-blotting; protein labeling (fluorescent, radio) and cross-linking; purification of proteins from *ex-vivo* sources.

Assay development

In vitro protein aggregation assays, cellular protein aggregation assays, microglia uptake assays, immunoprecipitation assays for epitope discovery in *ex-vivo* samples, various functional assays for proof-of-concept studies

LANGUAGES

English (advanced academic proficiency), Romanian (native), Hungarian (fluent), Spanish (intermediate) Dutch (intermediate)