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Research Topics

Applied to Life and Health Sciences

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Sport sciences and physical education

Topic #1

Effects of physical activity in cancer and in understanding the molecular mechanisms activated in response to different physical activity modalities

Leader: Pr Amélie Rébillard
amelie.rebillard@univ-rennes2.fr

Context

Adapted physical activity (APA) is now recognized as a non-drug therapeutic strategy for cancer patients (for review, Friedenreich and Courneya, book 2010, PMID: 21113758). The challenges of the coming years in the field of exercise oncology are to specify the recommendations in terms of PA for patients (Rapport expertise INSERM 2019, INCa 2017) and this naturally involves deciphering the molecular mechanisms.

Topic #1

Effects of physical activity in cancer and in understanding the molecular mechanisms activated in response to different physical activity modalities

Leader: Pr Amélie Rébillard
amelie.rebillard@univ-rennes2.fr

Aims

- Study the effects of physical activity on cancer depending on: i) the type of cancer; ii) the intensity of exercise; iii) its combination with other strategies.
- Understand the molecular mechanisms activated in response to different exercise modalities (immune system modulation, oxidative stress, epigenetic alterations).

Topic #1

Effects of physical activity in cancer and in understanding the molecular mechanisms activated in response to different physical activity modalities

Leader: Pr Amélie Rébillard
amelie.rebillard@univ-rennes2.fr

Experimental models

- Murine models of cancer : prostate cancer, colon cancer, pancreatic cancer.
- Physical activity interventions : wheel running, treadmill running.

Experimental techniques/methods

- Western blot, RT-qPCR, spectrofluorimetry, cell culture.

Topic #1

Effects of physical activity in cancer and in understanding the molecular mechanisms activated in response to different physical activity modalities

Leader: Pr Amélie Rébillard
amelie.rebillard@univ-rennes2.fr

Selected publications

- Gueritat, J., Lefeuvre-Orfila, L., Vincent, S., Cretual, A., Ravanat, J. L., Gratas-Delamarche, A., Rannou-Bekono, F., & Rebillard, A. (2014). Exercise training combined with antioxidant supplementation prevents the antiproliferative activity of their single treatment in prostate cancer through inhibition of redox adaptation. *Free radical biology & medicine*, *77*, 95–105. https://doi.org/10.1016/j.freeradbiomed.2014.09.009
- Dufresne, S., Guéritat, J., Chiavassa, S., Noblet, C., Assi, M., Rioux-Leclercq, N., Rannou-Bekono, F., Lefeuvre-Orfila, L., Paris, F., & Rébillard, A. (2020). Exercise training improves radiotherapy efficiency in a murine model of prostate cancer. FASEB journal : official publication of the Federation of American Societies for Experimental Biology, 34(4), 4984–4996. https://doi.org/10.1096/fj.201901728R
- Dufresne, S., Richard, C., Dieumegard, A., Orfila, L., Delpon, G., Chiavassa, S., Martin, B., Rouvière, L., Escoffre, J. M., Oujagir, E., Denis de Senneville, B., Bouakaz, A., Rioux-Leclercq, N., Potiron, V., & Rébillard, A. (2021). Voluntary Wheel Running Does Not Enhance Radiotherapy Efficiency in a Preclinical Model of Prostate Cancer: The Importance of Physical Activity Modalities?. Cancers, 13(21), 5402. https://doi.org/10.3390/cancers13215402

Topic #2

Effects of physical inactivity on skeletal muscle

Leader: Dr Frédéric Derbré
frederic.derbre@univ-rennes2.fr

Context

Extreme physical inactivity, as experienced by astronauts in microgravity conditions and by patients restricted to bed rest (e.g., Intensive care unit or aged patients) causes skeletal muscle wasting that directly impacts astronauts or patients' health. Our team especially focus on the underlying mechanisms of skeletal muscle wasting, with a focus on the crosstalk between muscle and gut microbiota or the main organ involved in iron metabolism (i.e. liver, spleen).

Topic #2

Effects of physical inactivity on skeletal muscle

Leader: Dr Frédéric Derbré
frederic.derbre@univ-rennes2.fr

Aims

- To understand structural and metabolic adaptations occurring in skeletal muscle promoting atrophy and insulin resistance in response to extreme physical inactivity.
- To characterize whether exercise or extreme physical inactivity (i.e. bed rest, microgravity) affects iron metabolism : iron distribution and hepcidin regulation, interactions between liver, spleen, and skeletal muscle.
- To characterize whether extreme physical inactivity and physical exercise affects gut microbiota composition and function, and the repercussions on skeletal muscle metabolism.

Topic #2

Effects of physical inactivity on skeletal muscle

Leader: Dr Frédéric Derbré
frederic.derbre@univ-rennes2.fr

Experimental models

- ***In vitro*** : murine C2C12 myoblasts, RAW macrophages.
- ***Pre-clinical (mice, rats)*** : tail suspension, wheel lock model, treadmill.
- ***Clinical*** : bed rest, dry immersion, acute exercise (treadmill, ergocyle).

Experimental techniques/methods

- Western blot, RT-qPCR, spectrofluorimetry.
- Histological analyses on skeletal muscle, liver and spleen.
- Shotgun sequencing (i.e. gut microbiota), ICP-MS (i.e. trace elements).

Topic #2

Effects of physical inactivity on skeletal muscle

Leader: Dr Frédéric Derbré
frederic.derbre@univ-rennes2.fr

Selected publications

- Horeau M, Ropert M, Mulder E, Tank J, Frings-Meuthen P, Armbrecht G, Loréal O, Derbré F. Iron Metabolism Regulation in Females and Males Exposed to Simulated Microgravity: results from the Randomized Trial AGBRESA. **Am J Clin Nutr**. 2022 Aug 26:nqac205. doi: 10.1093/ajcn/nqac205. Online ahead of print.
- Martin D, Nay K, Robin F, Rebillard A, Orfila L, Martin B, Leroyer P, Guggenbuhl P, Dufresne S, Noirez P, Ropert M, Loréal O, Derbré F. Oxidative and glycolytic skeletal muscles deploy protective mechanisms to avoid atrophy under pathophysiological iron overload. **J Cachexia Sarcopenia Muscle**. 2022 Apr;13(2):1250-1261. doi: 10.1002/jcsm.12897. Epub 2022 Feb 3.
- Jollet M, Nay K, Chopard A, Bareille M-P, Beck A, Ollendorff V, Vernus B, Bonnieu A, Mariadassou M, Rué O, Derbré F, Goustard B, Koechlin-Ramonatxo C. Does Physical Inactivity Induce Significant Changes in Human Gut Microbiota? New Answers Using the Dry Immersion Hypoactivity Model. **Nutrients** 2021 13(11):3865.
- Nay K, Koechlin-Ramonatxo C, Rochdi S, Island ML, Orfila L, Treffel L, Bareille MP, Beck A, Gauquelin-Koch G, Ropert M, Loréal O, Derbré F. Simulated microgravity disturbs iron metabolism and distribution in humans: lessons from dry immersion, an innovative ground-based human model. **FASEB** 2020 Sep 12 [Epub ahead of print]
- Nay K., Jollet M., Goustard B., Baati N., Vernus B., Pontones M., Lefeuvre-Orfila L., Bendavid C., Rué O., Mariadassou M., Bonnieu A. , Ollendorff V., Lepage P., Derbré F., Koechlin-Ramonatxo C. Gut bacteria are critical for optimal muscle function: a potential link with glucose homeostasis**. Am J Physiol End Meta**. 2019 Jul 1;317(1):E158-E171.

Topic #3

e-Health and digital innovation in physical behavior measurement

Leader: Dr Alexis Le Faucheur
alexis.lefaucheur@ens-rennes.fr

Context

A key point in the contemporary studies of the relationship between physical behavior and health, is the precise assessment of physical behavior, which is complex due to its multidimensional nature.
The use of activity monitors provides a unique opportunity to catch this multifaceted nature of physical behavior both for health and disease applications, but valid tools and methodological advances are required.

Topic #3

e-Health and digital innovation in physical behavior measurement

Leader: Dr Alexis Le Faucheur
alexis.lefaucheur@ens-rennes.fr

Aims

- Study the validity of activity monitors and processing methods in measuring Human physical behavior, including the related energy expenditure.
- Determine the “digital profile” in terms of daily and free-living physical behavior/walking pattern in people with clinical conditions and identify specific metrics that could provide potential relevant clinical information and improve patients care.
- Test and develop digital solutions to implement physical activity based therapeutic interventions.

Topic #3

e-Health and digital innovation in physical behavior measurement

Leader: Dr Alexis Le Faucheur
alexis.lefaucheur@ens-rennes.fr

Experimental context

- Free-living and prolonged measurement of physical activity (~ 7 days).
- Standardized or semi-standardized physical activities (walking).

Experimental techniques/methods

- Activity monitors : accelerometer, pedometer, GPS devices.
- Gas exchange measurement
- Data processing and signal analysis
- Digital devices and app

Topic #3

e-Health and digital innovation in physical behavior measurement

Leader: Dr Alexis Le Faucheur
alexis.lefaucheur@ens-rennes.fr

Selected publications

- Taoum A, Chaudru S, DE Müllenheim PY, Congnard F, Emily M, Noury-Desvaux B, Bickert S, Carrault G, Mahé G, LE Faucheur A. Comparison of Activity Monitors Accuracy in Assessing Intermittent Outdoor Walking. Med Sci Sports Exerc. 2021 Jun 1;53(6):1303-1314. doi: 10.1249/MSS.0000000000002587. PMID: 33731660.
- Le Faucheur A, Abraham P, Jaquinandi V, Bouyé P, Saumet JL, Noury-Desvaux B. Measurement of walking distance and speed in patients with peripheral arterial disease: a novel method using a global positioning system. Circulation. 2008 Feb 19;117(7):897-904. doi: 10.1161/CIRCULATIONAHA.107.725994. Epub 2008 Feb 4. PMID: 18250268.
- Le Faucheur A, Noury-Desvaux B, Mahé G, Sauvaget T, Saumet JL, Leftheriotis G, Abraham P. Variability and short-term determinants of walking capacity in patients with intermittent claudication. J Vasc Surg. 2010 Apr;51(4):886-92. doi: 10.1016/j.jvs.2009.10.120. PMID: 20347684.
- Chaudru S, Jehannin P, de Müllenheim PY, Klein H, Jaquinandi V, Mahé G, Le Faucheur A. Using wearable monitors to assess daily walking limitations induced by ischemic pain in peripheral artery disease. Scand J Med Sci Sports. 2019 Nov;29(11):1813-1826. doi: 10.1111/sms.13511. Epub 2019 Jul 31. PMID: 31271680.

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Mathematics

Stochastic regulatory networks

Leader: Pr Arnaud Debussche
arnaud.debussche@ens-rennes.fr

Context

Stochastic simulation of gene networks by Markov processes has important applications in molecular biology. The complexity of exact simulation algorithms scales with the number of discrete jumps to be performed. Approximate schemes reduce the computational time by reducing the number of simulated discrete events. Reduced model have been derived in various cases: ODEs in large volume limit for well stirred system, piecewise deterministic Markov processes (PDMP) for multiscale systems, PDEs and infinite dimensional PDMPs when spatial dependance is taken into account.

Stochastic regulatory networks

Leader: Pr Arnaud Debussche
arnaud.debussche@ens-rennes.fr

Aims

Consider multiscale spatially dependent systems and derive reduced models under realistic biological assumptions and in various situations. Study the qualitative behavior of the reduced model.

Stochastic regulatory networks

Leader: Pr Arnaud Debussche
arnaud.debussche@ens-rennes.fr

Selected publications

- Crudu, A., Debussche, A., Radulescu, O.: Hybrid stochastic simplifications for multiscale gene net- works. BMC Syst. Biol. 3, 89 (2009)
- Crudu, A., Debussche, A., Muller, A., Radulescu, O.: Convergence of stochastic gene networks to hybrid piecewise deterministic processes. Ann. Appl. Probab. 22(5), 1822–1859 (2012)
- Debussche, A., Nguepedja Nankep, M.J.: A Law of Large Numbers in the Supremum Norm for a Multiscale Stochastic Spatial Gene Network. Int. J. Biostat. 15(2), 20170091 (2019)
- Debussche, A., Nguepedja Nankep, M.J.: A piecewise deteministic limit for a multiscale stochastic spatial gene network, AMO, 84, 1731-1767, (2021)

BIOSANTEXC

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Environmental Sciences

GEOSCIENCES Rennes

ECOBIO Rennes

Environmental consequences of antibiotics: How do antibiotics interfere with the bacteria of the N-cycle in natural waters?

Leader: Dr Camille Vautier
camille.vautier@ens-rennes.fr

Context

Human and veterinary medicine induces the release of antibiotics in natural waters, trough the spreading of animal dejections on the fields, or through the contamination of sewage. Designed to fight pathogenic bacteria, antibiotics can, once in the environment, impact bacteria different from their initial target. Especially, studies show that some antibiotics can have negative impact on denitrifying bacteria. These bacteria are crucial to reduce nitrate pollution, responsible for the eutrophication in coastal zones.

Environmental consequences of antibiotics: How do antibiotics interfere with the bacteria of the N-cycle in natural waters?

Leader: Dr Camille Vautier
camille.vautier@ens-rennes.fr

Scientific questions

While some laboratory experiments show the potential impact of antibiotics on denitrifying bacteria, their effect in the natural conditions of the environment remains to be studied. Indeed, the concentration of antibiotics in groundwater and rivers is well below therapeutic levels.

Are antibiotic concentrations in the natural environment sufficient to have an effect on denitrifying bacteria? Does the exposure time in the aquifer cause a long-term effect? What is the overall effect of antibiotics on the nitrogen cycle?

Environmental consequences of antibiotics: How do antibiotics interfere with the bacteria of the N-cycle in natural waters?

Leader: Dr Camille Vautier
camille.vautier@ens-rennes.fr

Scientific methodology

The project will combine field work, laboratory experiments and modelling:

- measurements of nitrates and antibiotics in rivers and groundwater to determine their localization in the environment.
- experiments in continuous flow reactors to characterize the action of antibiotics on bacteria of the nitrogen cycle.
- numerical modelling to upscale laboratory results, with the objective of assessing environmental risks on a large scale.

Environmental consequences of antibiotics: How do antibiotics interfere with the bacteria of the N-cycle in natural waters?

Leader: Dr Camille Vautier
camille.vautier@ens-rennes.fr

Selected publications

- Charuaud, L. et al. Veterinary pharmaceutical residues in water resources and tap water in an intensive husbandry area in France. Science of The Total Environment 664 (2019). doi:10.1016/j.scitotenv.2019.01.303
- Liu, Y. et al. Modeling the Fate of Pharmaceuticals in a Fourth-Order River Under Competing Assumptions of Transient Storage. Water Resources Research 56 (2020). doi:10.1029/2019WR026100
- Laverman, AM. et al. Exposure of vancomycine causes a shift in the microbial community structure without effecting nitrate reduction rates in river sediments. Environmental Science and Pollution Research 22 (2015). doi:10.1007/s11356-015-4159-6
- Roose-Amsaleg, C. & Laverman, AM. Do antibiotics have environmental side-effects? Impact of synthetic antibiotics on biogeochemical processes. Environ Sci Pollut Res Int 23 (2016). doi:10.1007/s11356-015-4943-3