Comité de gestion de la Chaire

Famille Jean-Guy Sabourin

5 Juillet 2022

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Chercheur CRCHUM
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Une étude d'AstraZeneca indique que la thérapie anti-CD73, développée par John Stagg, augmente l'efficacité du traitement anti-PD-L1 chez les patients atteints de cancer du poumon

22 septembre 2021

Notre professeur avait découvert que l'enzyme CD73 contribue à la progression du cancer en 2010.

Lui et son équipe au CRCHUM ont été les premiers à démontrer que les anticorps dirigés contre CD73 bloquent la production d'adénosine extracellulaire et agissent comme des agents anti-tumoraux capables d'augmenter l'activité des inhibiteurs de points de contrôles anti-PD-1.

Ses découvertes ont mené au développement de plusieurs agents thérapeutiques ciblant la voie de l'adénosine. M. Stagg a, entre autres, collaboré avec la pharmaceutique AstraZeneca dans le développement de l'oleclumab, un anticorps monoclonal ciblant CD73.

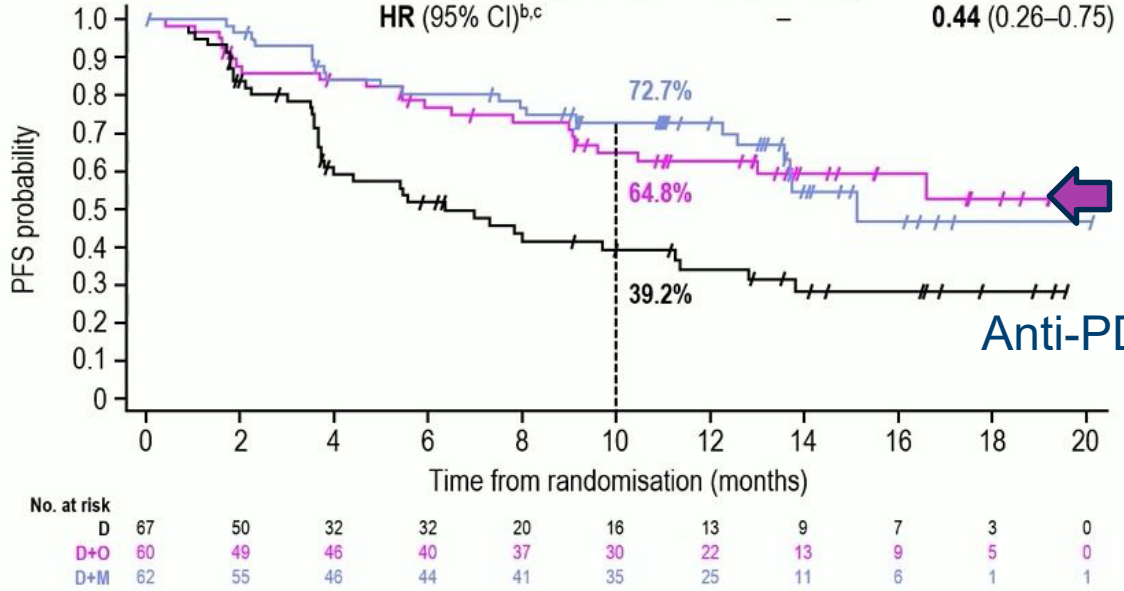
Les résultats préliminaires d'AstraZeneca sont très encourageants pour cette nouvelle classe de médicaments issue des découvertes du Dr Stagg.

Étude de Phase 2 randomisée:

PFS by investigator assessment (interim analysis; ITT population)

Anti-PDL1 | Anti-PDL1+ Anti-CD73 | Anti-PDL1+ Anti-NKG2A

	D	D+O	D+M
Events/patients, n	38/67	22/60	21/62
mPFS, months (95% CI)[a]	**6.3** (3.7–11.2)	**NR** (10.4–NE)	**15.1** (13.6–NE)
HR (95% CI)[b,c]	–	**0.44** (0.26–0.75)	**0.65** (0.49–0.85)



Anti-PDL1+ Anti-CD73 (oleclumab)

Anti-PDL1

No. at risk											
D	67	50	32	32	20	16	13	9	7	3	0
D+O	60	49	46	40	37	30	22	13	9	5	0
D+M	62	55	46	44	41	35	25	11	6	1	1

Data cutoff: 17 May 2021 (median follow-up of 11.5 months; range, 0.4–23.4)

[a]Interim analysis was performed when all patients had a 10-month minimum potential follow-up; Kaplan-Meier estimates for PFS, PFS rate and 95% CIs

[b]PFS HR and 95% CI estimated by Cox regression model, stratified by histology (adenocarcinoma and non-adenocarcinoma)

[c]Compared with the 67 and 64 patients in the D arm enrolled concurrently with patients in the D+O and D+M arms, respectively

CI, confidence interval; HR, hazard ratio; ITT, intention to treat; mPFS, median PFS; NE, not estimable; NR, not reached

2021 ESMO congress

Cancer du sein Triple Négatif

SYNERGY: Phase I and randomized phase II trial to investigate the addition of the anti-CD73 antibody oleclumab to durvalumab, paclitaxel and carboplatin for previously untreated, locally recurrent inoperable or metastatic triple-negative breast cancer (TNBC)

C. Maurer • D. Eiger • C. Velghe • P.G. Aftimos • M. Maetens • J. Gaye • M. Paesmans • M. Ignatiadis • M. Piccart • L. Buisseret • Show less

Début de la Phase 3 en poumon (NSCLC, stage 3)

A Global Study to Assess the Effects of Durvalumab (anti-PDL1) With Oleclumab (anti-CD73) or Durvalumab With Monalizumab (anti-NKG2A) Following Concurrent Chemoradiation in Patients With Stage III Unresectable Non-Small Cell Lung Cancer (PACIFIC-9)

Sept professeurs de l'UdeM figurent parmi les plus cités au monde par leurs pairs

UDEMNOUVELLES | LE 19 NOVEMBRE 2021

EN 5 SECONDES

Les professeurs Étienne Laliberté, Vincent Larivière, Pierre Legendre, Jean-Claude Moubarac, Fred Saad, John Stagg et Mike Tyers font briller notre université!

Publications depuis le dernier comité

1 CD73 inhibits cGAS-STING and cooperates with CD39 to promote pancreatic cancer. Foissac C, Bareche Y, Cousineau I, Pommey S, Chrobak P, Robson SC, Turcotte S, **Stagg J**.. **Can Immunol Res 2022 (in press)**.

2 Leveraging Big Data of Immune Checkpoint Blockade Response Identifies Novel Potential Targets. Bareche Y, Kelly D, Abbas-Aghababazadeh F,.., Haibe-Kains B, **Stagg J. Annals Oncol 2022 (in revision)**.

3 Adenosine A2A receptor is a tumor suppressor of NASH-HCC. Bertrand Allard, Célia Jacoberger-Foissac, ... and **Stagg J. Gut 2022 (in revision)**

4 Spatially mapping the immune landscape of melanoma using imaging mass cytometry. Moldoveanu D, Ramsay L, Lajoie M, Anderson-Trocme L,..., **Stagg J**, Quail DF, Mihalcioiu C, Meterissian S, Watson IR. **Sci Immunol. 2022 Apr;7(70):eabi5072**.

5 Prognostic implications of adaptive immune features in MMR-proficient colorectal liver metastases classified by histopathological growth patterns. Messaoudi N, Henault D, Stephen D, Cousineau I, Simoneau E, Rong Z, Létourneau R, Plasse M, Dagenais M, Roy A, Lapointe R, Vandenbroucke-Menu F, Kunda R, Ysebaert D, Soucy G, **Stagg J**, Vermeulen P, Turcotte S**. Br J Cancer. 2022 May;126(9):1329-1338.**

6 High-dimensional analysis of the adenosine pathway in high-grade serous ovarian cancer. Bareche Y, Pommey S, Carneiro M, Buisseret L, Cousineau I, Thebault P, Chrobak P, Communal L, Allard D, Robson SC, Mes-Masson AM, Provencher D, Lapointe R, **Stagg J.** J **Immunother Cancer. 2021 Mar;9(3):e001965**.

7 DNA hypomethylating agents increase activation and cytolytic activity of CD8+ T cells. Loo Yau H, Bell E, ..., **Stagg J**, Brooks DG, De Carvalho DD. **Mol Cell. 2021 Apr 1;81(7):1469-1483.e8.**

8 1-Methylnicotinamide is an immune regulatory metabolite in human ovarian cancer. Kilgour MK, MacPherson S, Zacharias LG, Ellis AE, Sheldon RD, Liu EY, Keyes S, Pauly B, Carleton G, Allard B, Smazynski J, Williams KS, Watson PH, **Stagg J**, Nelson BH, DeBerardinis RJ, Jones RG, Hamilton PT, Lum JJ. **Sci Adv. 2021 Jan 20;7(4):eabe1174.**

9 Microbiome-derived inosine modulates response to checkpoint inhibitor immunotherapy. Mager LF, Burkhard R, Pett N, Cooke NCA, Brown K, Ramay H, Paik S, **Stagg J**, Groves RA, Gallo M, Lewis IA, Geuking MB, McCoy KD. **Science. 2020 Sep 18;369(6510):1481-1489.**

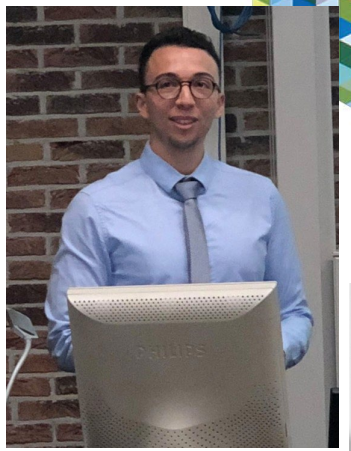
Nouveaux financements

CIHR Operating Grant (2022-2027): $1,000,000

Surface Oncology Research Grant (2022-2024): $ 300,000

Domain Therapeutics Research Grant (2022-2024): $ 250,000

IVADO postdoctoral salary support (2022): Yacine Bareche, Ph.D.



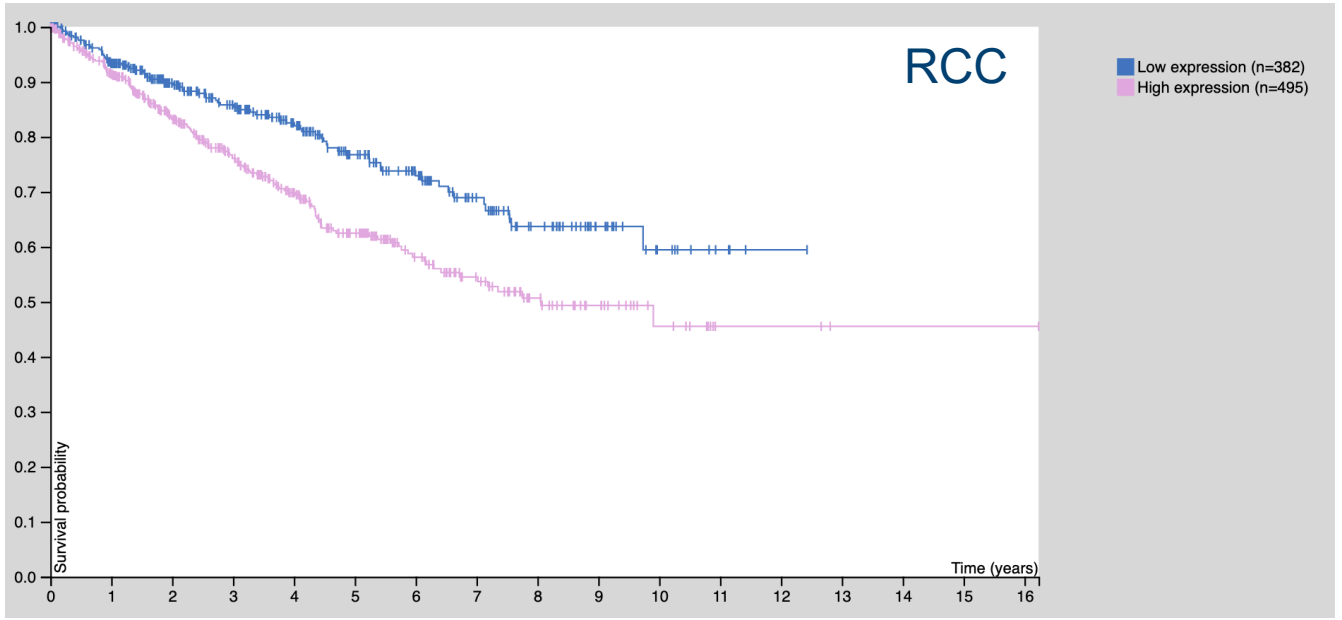
MITACS postdoctoral fellowship (2022-2023): Célia Jacoberge-Foissac, Ph.D.

TRANSCAN-3 (2022-2025): $ 250,000

MAGNOLIA: MAppinG adaptatioN Of tripLe negative breast cancer microenvironments to ImmunotherApy

- 6 partners from 4 countries (Canada, France, Belgium, Germany) with the common vision of aligning cancer research and innovation programs

Hypothesis: ENT1 expression in tumor cells favors release of excess Adenosine in the extracellular environment, which suppressed anti-tumor immunity



ENT1 is associated with worse cancer prognosis

Experimental Plan:

1. Which tumor cell lines overexpress ENT1?
2. What is the impact of ENT1 gene-targeting in tumor cells?
    - on extracellular Adenosine levels;
    - on activation of Adenosine receptors;
    - on tumor-infiltrating immune cells;
    - on immune checkpoint therapy

3. What human tumors express ENT1 (is it associated with other biomarkers, e.g. ADK, CD73)

4. Will an inhibitor of ENT1 have antitumor activity?
    - is it immune-dependent
    - is it equal to blocking Adenosine A2a/b receptors
    - can we develop a therapeutic antibody

Requested Budget: $50K