Journal of Clinical and Medical Research

ISSN: 2582-4333
Hernández-Bronchud M, 2022-J Clin Med Res
Short Review

Redeployment of Placental Gene Programming: Can Invasive Placentation Molecular Switches Complement the Hallmarks of Cancer?

Miguel Hernández-Bronchud*

COMB 23515, Génesis Care Corachan, Barcelona, Plaza Dr. Manuel Corachan 1, 08017 Barcelona, Spain

***Corresponding Author:** Miguel Hernández-Bronchud, COMB 23515, Génesis Care Corachan, Barcelona, Plaza Dr. Manuel Corachan 1, 08017 Spain.

Received Date: 08-27-2022

Accepted Date: 09-28-2022

Published Date: 10-11-2022

Abstract

Placentation arose in mammalian evolution some 150-200 M years ago and integrates in a rather ingenious manner a large number of previously evolved multicellular regulatory pathways which include: angiogenesis, inflammatory cytokines and interleukins, HLA expression, immune peptides, immune regulatory receptors (for NK decidual cells, T and B cells, including Tregs, macrophages, antigen-presenting cells), endothelial cells and fibroblasts, immune checkpoints (including PD-L1), many paracrine or endocrine hormones and growth factors, tissue enzymes, extracellular vesicles, several different mechanisms for epithelial-mesenchymal transitions, several hypoxia adaptations, morphogenetic changes, and others. Speculating from real genomics and epigenetic data from a single clinical case of a pregnant young woman with breast cancer, it has been recently proposed that mammalian cancer cells do not have to invent "de novo" immune escape mechanisms, including so-called "immune editing", but to redeploy–probably by epigenetic mechanisms–intrinsic or encrypted gene programmes physiologically used by the process of invasive placentation in mammals. Most of these programmes were not evolved specifically for the placenta–but there were probably some exceptions, such as those still poorly understood key pathways related to foeto-maternal tolerance or perhaps trophoblast differentiation and decidual invasion. In my opinion, invasive placentation molecular switches can complement the hallmarks of cancer, by re-using "placental gene programming" to the competitive advantage of cancer cells.

Keywords: Redeployment; Gene programming; Placentation; Cancer.

Citation: Hernández-Bronchud M. Redeployment of Placental Gene Programming: Can Invasive Placentation Molecular Switches Complement the Hallmarks of Cancer?. J Clin Med Res. 2022;4(5):1-9.
DOI: https://doi.org/10.37191/Mapsci-2582-4333-4(5)-123

Introduction

'Hallmarks of Cancer' was the title of a review published in 'Cell' by Dr. Douglas Hanahan and Dr. Robert Weinberg early in the year 2000 [1] and which is so far one of the most important papers published in cancer biology. To find a common denominator of cancer they set up a conceptual framework for tumour development. It constitutes a collection of 'acquired capabilities and characteristics' of neoplastic malignancy. These "cancer hallmarks" have been gradually updated from the original six [1] to ten hallmarks in 2011 and fourteen in the latest addition in 2022 [2,3]. Following the experimental demonstration in one clinical case of a pregnant woman with breast cancer diagnosed towards the end of her pregnancy [4–10], it was suggested that re-using "placental gene programming" (to the competitive advantage of cancer cell clones) can help tumour cells to escape from immune vigilance during carcinogenesis, or cancer progression. Our analysis (published in 2016-2020) was carried out in primary breast cancer with metastatic homolateral axillary lymph nodes as well as placenta tissue (both uterine decidual tissue and term placenta tissue) from a pregnant woman with twins who was diagnosed with lobular infiltrating breast cancer towards the end of her pregnancy and following caesarean section (prior to mastectomy and lymphadenectomy almost twenty years ago) required a hysterectomy due to excessive bleeding. Following surgery the patient received adjuvant chemotherapy with dose-dense chemotherapy and filgrastim (G-CSF) support. Both the mother and her two children are well and healthy at present. Gene expression profiling of paired non-self and self-tissues (i.e., placenta/uterus; breast cancer/normal breast tissue; metastatic lymph node/normal lymph node tissue) was performed using the Pan Cancer Immune gene panel, a 770 Nanostring (Seattle, USA) gene expression panel. Our findings revealed significant overlapping in specific immune gene expression in placenta and cancer tissue, suggesting that these genes might play an important role in maintaining immune tolerance both physiologically (in the placenta) and pathologically (in the cancer setting) [4–10]. The same tissues were analysed by epigenomic analysis of these tissue samples and described the main findings with respect to immune-related gene regulation (over- or under-expressed) in cancer cells as compared to placental tissues. The [5] significant similarities, and hierarchical clustering (both unsupervised and supervised) were confirmed in CpG island methylation patterns between decidual/placental and cancer microenvironments, which cannot be easily explained by simple models or unique pathways. Supervised CpG island methylation hierarchical clustering heat-maps showed a consistently differential methylation pattern that was closer between normal tissues (breast and normal lymph nodes) than between normal and malignant tissues, or placental decidual tissues. Several different cell types are probably involved in these complex immune regulation mechanisms. Cancers, it was concluded, may somehow "hijack" gene programmes evolved over millions of years to allow for foeto-maternal tolerance in placental mammals in order to escape from immune vigilance and spread locally or to distant sites. Once a cancer

Citation: Hernández-Bronchud M. Redeployment of Placental Gene Programming: Can Invasive Placentation Molecular Switches Complement the Hallmarks of Cancer?. J Clin Med Res. 2022;4(5):1-9.
DOI: https://doi.org/10.37191/Mapsci-2582-4333-4(5)-123

micro-environment has acquired the genetic and epigenetic "placental immune editing switches" (PIES) phenotype-as we call these immune regulatory genes or epigenetic markers shared between malignant and placental tissues-it seems likely that this will keep them "available", whenever needed, for the rest of cancer development, as presumably they confer on cellular clones the competitive advantage of passing unnoticed by the host's immune system. This “cancer invisibility” should allow primary cancers and their metastases to continue growing in spite of dynamic antigenic landscapes.

Dunn and colleagues [11–13] proposed in 2002-2004 that most cancers underwent immunoediting, from immunosurveillance, through “equilibrium”, to tumour escape. The placental immune editing switches (PIES) hypothesis proposed a broad and evolutionary framework [4–10] for the molecular mechanisms of cancer immune editing by postulating that many of them could be related to ancient evolutionary mechanisms related to foeto-maternal immune tolerance mechanisms in placental mammals. Experimental and clinical evidence has been published on cancer immune editing [14]. It seems likely that during carcinogenesis and cancer progression there are T-cell-dependent and T-cell-independent mechanisms of cancer immunoediting. It was hypothesized that much of what people know about immunoediting in cancer cells will be relevant to why the placental allograft is tolerated by the mother. Conversely, some insights may gain into how cancers evade the host immune system from what was learnt from pregnancy.

Cancers, while occupying a microenvironment teeming with immune cells, utilize a wide range of tactics that impede anti-tumour immunity and even divert immune cell activities to their own advantage [14,15]. For example, certain cancer cells are capable of secreting immunosuppressive factors targeted to various immune cell types, possibly, as in cancer, causing cytotoxic T-cells to become hyporesponsive. Other cancers reduce their expression of surface exposed MHC Class I and II and T-cell receptor co-stimulatory molecules. They may also process or present antigens poorly. These mechanisms, because of their breadth, are not extensively discussed here, although they also seem to represent strategies used by placental trophoblast. On the other hand, immunotherapies have transformed cancer treatments over the past decade, even if resistance mechanisms are still poorly understood [16–22]. James Allison and Tasuko Honjo shared the 2018 Nobel Prize for Physiology or Medicine for their pioneering contributions to these transforming cancer treatments. Although checkpoint inhibitors approved for clinical use have so far been confined to those that target PD-1 or its ligand PD-L1 and CTLA-4, others directed against additional checkpoint components are currently in clinical trials, and some have been reported in placental tissues, including trophoblasts [23–32]. HLA-G, better known for its expression in extravillous trophoblast, is also associated with several forms of malignant cancer cells [23]. Unfortunately, there is only limited supporting evidence for immune checkpoints contributing to trophoblast defence in mice genetics [30].

Citation: Hernández-Bronchud M. Redeployment of Placental Gene Programming: Can Invasive Placentation Molecular Switches Complement the Hallmarks of Cancer?. J Clin Med Res. 2022;4(5):1-9.
DOI: https://doi.org/10.37191/Mapsci-2582-4333-4(5)-123

The mysterious origin of invasive placentation

The emerging field of "Paleovirology" [33] has led to the discovery that syncytins are 'new' genes encoding proteins derived from the envelope protein of endogenous retroviral elements that have been independently captured (on repeated occasions) in different mammalian species by a process of "convergent evolution". A "convergent evolution" was also postulated by Wagner's group [34] to suggest that mammals with the most invasive types of placenta also have higher cancer risks. According to their original observations, this is mainly due to a higher degree of stromal "invasibility", rather than tumour "invisibility" [34]. Knockout experiments on syncytin genes in mice (nicely reviewed in ref. 33) provide evidence that they are essential for placenta development and survival of the embryo by cell–cell fusion of syncytial cell layers at the foetal–maternal interface.

The issue of choriocarcinomas

Placental trophoblast behaviour (e.g., extra villous villi) is invasive, but not malignant. Lala et al. [35] have recently published an elegant review in 'Placenta J.', stressing the differences rather than the similarities between placenta and cancer. For example, placenta invasion is tightly controlled, whereas tumour invasion evades this control. The genomics of choriocarcinomas [36] indicate that their gene drivers are probably different from those of most human epithelial cancers. Normal trophoblasts somehow retain normal physiological mechanisms of cellular proliferation, and local or distant invasion control. Choriocarcinoma cells are genomically different from trophoblasts because, like all malignant tumours, they accumulate specific carcinogenic mutations, unlike invasive normal trophoblasts that do not, and they continue to respond to physiological signals that prevent them from truly invading not only the decidual tissues but also neighbouring local tissues, and from spreading by blood or lymphatic systems to distant sites. Recently, Jung et al. [36] have detected five driver mutations in gestational choriocarcinomas, GCs, most of which were chromatin remodelling gene (ARID1A, SMARCD1, and EP300) mutations, but not mutations in common cancer gene drivers such as TP53 and KRAS. Most GCs (25/29) harbouring recurrent copy number alterations (CNAs), and gains on 1q21.1-q44 were significantly associated with poor prognoses. Interestingly, copy-neutral loss-of-heterozygosity (CN-LOH) is an apparent early pivotal event in hydatidiform mole to gestational choriocarcinomas (HM-IM-GC) development, and CNAs may be a late event that promotes progression to GC. Their [36] data indicate that GCs have unique profiles of CN-LOHs, mutations and CNAs that together differentiate GCs from non-GCs. CN-LOH and CNA profiles will probably be useful for the molecular diagnosis of GC and for the selection of GC patients with poor prognoses for more intensive chemotherapy treatments, respectively. The fact that choriocarcinomas do not primarily depend on frequently mutating gene drivers (unlike most common human epithelial cancers) is intriguing. On balance, it seems reasonable to speculate that trophoblasts do not "hijack" invasive placentation epigenetic switches (whatever their nature might be) through mutated cancer gene drivers, but probably by

Citation: Hernández-Bronchud M. Redeployment of Placental Gene Programming: Can Invasive Placentation Molecular Switches Complement the Hallmarks of Cancer?. J Clin Med Res. 2022;4(5):1-9.
DOI: https://doi.org/10.37191/Mapsci-2582-4333-4(5)-123

physiological and still unknown regulatory mechanisms-quite probably including specific transcription factor networks.

Immune suppressive effects of mutated 'gene drivers'

A fairly comprehensive review has been recently published in 'Oncogene' on how oncogenes and other cancer gene drivers (including tumour suppressor genes) can elicit immune escape mechanisms, and how cytotoxic and targeted therapies (including PD-L1) partially reverse these effects [37]. Curiously, though, these authors from Nashville USA do not relate any of these interesting immune escape mechanisms-by viral and non-viral-related cancers-to that magic and often forgotten organ: the placenta. Even though, first, the placental organ might have evolved precisely from a retroviral infection (or probably several successive retroviral infections) starting some 150 M years ago (the origin of mammals with invasive placenta); secondly, one of the functions of the placenta is precisely to defend the foetus from foreign pathogens, including viruses; and thirdly, another of the functions of the placenta is the "maternal-foetal tolerance", that is, the immune escape of the foetus from the maternal immune system.

Transcription Factors and Placentation

It seems quite probable that the co-ordinated actions of transcription factors (TFs) regulate trophoblast cell types, including syncytiotrophoblast and extravillous trophoblast [38]. A recent review of the expression of repetitive elements (REs), endogenous retroviruses (ERVs) and transposable elements (TEs) in cells of the placenta and in cancer, related to changes in malignant phenotype and immune regulation, has been published by a research group in New Zealand [39]. A comparative study by Nordor et al. (2017) [40] identified that almost half of the hypomethylated DNA regions in placentation overlapped with hypomethylated DNA regions in several different cancer types, when comparing DNA methylation similarities between cancer cells and first trimester placenta. It has also been suspected for some time [41] that transposable elements (TE) drive widespread expression of oncogenes in human cancers; or that endogenous retrovirus function as species-specific enhancer elements in the placenta [42,43]. As recently pointed out by Illsley et al. [44], probably only the differentiation of cytotrophoblast (CTB) into the invasive extravillous trophoblast (EVT) has been clearly identified, suggesting a key role for the transcription factor ZEB_2 (zinc finger E-box binding protein 2) in the relevant epithelial-mesenchymal transition (EMT). Perhaps surprisingly, a recent single-cell survey of the human first trimester placenta and decidua [45]–based on single-cell transcriptomics of specific cell markers–suggests a possible role shift of EVTs from being mainly anti-inflammatory in the early stages of pregnancy. However, a number of papers point to a more complex and interactive dynamic networks of TFs:

1. There is one interesting article that compares transcriptomes in cancer and preeclamptic placenta "Roxana Moslehi, James L. Mills, Caroline Signore, Anil Kumar, Xavier Ambroggio & Amiran Dzutsev,

Citation: Hernández-Bronchud M. Redeployment of Placental Gene Programming: Can Invasive Placentation Molecular Switches Complement the Hallmarks of Cancer?. J Clin Med Res. 2022;4(5):1-9.
DOI: https://doi.org/10.37191/Mapsci-2582-4333-4(5)-123

Integrative transcriptome analysis reveals dysregulation of canonical cancer molecular pathways in placenta leading to preeclampsia, Scientific Reports , 30 aug, 2013, 2407 | DOI: 10.1038/srep024071

2. Regarding the roles of HLA-G expression by EVT and many Cancer cells, here is a good review: "Lin A, Yan WH. Human Leukocyte Antigen-G (HLA-G) Expression in Cancers: Roles in Immune Evasion, Metastasis and Target for Therapy. Mol Med. 2015 Nov;21(1):782-791. doi: 10.2119/molmed.2015.00083. Epub 2015 Aug 24. PMID: 26322846; PMCID: PMC4749493."
3. Perhaps surprisingly, a recent single-cell survey of the human first trimester placenta and decidua [45]-based on single-cell transcriptomics of specific cell markers-suggests a possible role shift of EVTs from being mainly anti-inflammatory in the early stages of pregnancy. The authors find that there are marked regional differences in differentiation pathways of CTB into STB and EVT between the smooth chorion (SC) and Villous chorion sampled from a a mid-gestational placenta. SC-CTBs forma a stratified epithelium and show distinct expression of cytokeratin isoforms like the epidermis, secrete migration-inhibitory factors. EVTs in the SC are essentially non-migratory, remaining close to the CTBs.

Other transcription factors are also worth following up in this context. For example, NALP7 is the first maternal effect gene-identified in humans and is also responsible for recurrent spontaneous abortions, stillbirths, and intra-uterine growth retardation [46]. It is also part of a key TF (transcription factor) family with many functionalities, ranging from immune control to placental tumours (moles) [47–49]. NLRP7, for example, is involved in hydatidiform molar pregnancy, and interacts with the transcriptional repressor ZBTB16.

Conclusions and future suggestions

At present, the definitive immune regulatory mechanisms of foeto-maternal tolerance are not understood in mammals with invasive placentation, nor the immune regulatory mechanisms of immune vigilance or immune escape during carcinogenesis or cancer progression. “Eppur si muove”-Galileo might say. And yet, “they happen”. Whether or not the two key biological processes are mechanistically molecularly related remains to be proved experimentally (beyond our single clinical case with comprehensive genomic and epigenomic studies). But further experimental research, pre-clinical and clinical, on the hypothesis of redeployment of placental gene programmes, is warranted. Pre-clinical models are being contemplated at present, ranging from rodents (mice and rats, inducing cancers by chemical/hormonal sequencing and then made pregnant- or genetically suitably modified strains) to others. The review article is not conceptually flawed. On the

Citation: Hernández-Bronchud M. Redeployment of Placental Gene Programming: Can Invasive Placentation Molecular Switches Complement the Hallmarks of Cancer?. J Clin Med Res. 2022;4(5):1-9.
DOI: https://doi.org/10.37191/Mapsci-2582-4333-4(5)-123

contrary, most reviewers agree it does introduce several new unpublished concepts that unfortunately require more in-depth experimental evidence.

Unfortunately, to find substantial more clinical cases like the single one (pregnant woman with breast cancer)-with six relevant tissues of the same individual patient for direct comparisons, including uterus and placental decidual tissues-is very difficult. Equally difficult might prove to study experimentally breast carcinogenesis in Platypuses Ornitorhincus or Equidna (Australian ancestral mammals in risk of extinction and difficult to work with in the labs). Fascinating mammals-without placental tissues that in spite of breast ducts or lobules do not appear to get breast cancers. Controversy always existed on the utility of chemically induced mouse or rat mammary carcinogenesis models as valid equivalents for the study of human breast cancer. But in order to attempt to reproduce my results on the genomics and Epigenetic parallelism such preclinical rodents' models might provide us with interesting data. For example, models of carcinogenic relevance (combined chemical carcinogenic substances with hormonal progesterone-like stimulation to induce pregnancy), or others based on genetically modified mice strains, could provide us with a "gold mine of new data" linking mammalian invasive placentation to breast cancer, and possibly other cancers too. Comparative bio information analysis of Genomic and Epigenetic signatures in normal tissues, decidual and placental tissues and cancers in experimental pregnant animals, will offer a complex but fuller insight into carcinogenesis, cancer progression and cancer hallmarks, as well as on the mystery of the evolutionary development of frequent epithelial cancers.

References

1. Hanahan D, Weinberg RA. The hallmarks of cancer. Cell. 2000;100(1):57-70. PubMed | CrossRef
2. Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. Cell. 2011;144(5):646-74. PubMed | CrossRef
3. Hanahan D. Hallmarks of cancer: new dimensions. Cancer Discov. 2022;12(1):31-46. PubMed | CrossRef
4. Bronchud MH, Tresserra F, Xu W, Warren S, Cusido M, Zantop B, et al. Placental immune editing switch (PIES): learning about immunomodulatory pathways from a unique case report. Oncotarget. 2016;7(50):83817. PubMed | CrossRef
5. Bronchud MH, Tresserra F, Zantop BS. Epigenetic changes found in uterine decidual and placental tissues can also be found in the breast cancer microenvironment of the same unique patient: description and potential interpretations. Oncotarget. 2018;9(5):6028. PubMed | CrossRef
6. Hernández-Bronchud M. Alpha and Omega: from the Sagrada Familia to Placenta and Cancer. CrossRef
7. M. Hernández-Bronchud, Placental immune editing switches (PIES) and cancer progression. Research Outreach. 2020. CrossRef
8. Hernández-Bronchud M. Do locally advanced and metastatic human epithelial cancers evolve in 'placental/decidual-like microenvironments'?. Clin Transl Oncol. 2019;21(2):160-6. PubMed | CrossRef
9. Bronchud MH. Are aggressive epithelial cancers 'a disease'of Eutherian mammals?. Ecancermedicalscience. 2018;12. PubMed | CrossRef

Citation: Hernández-Bronchud M. Redeployment of Placental Gene Programming: Can Invasive Placentation Molecular Switches Complement the Hallmarks of Cancer?. J Clin Med Res. 2022;4(5):1-9.
DOI: https://doi.org/10.37191/Mapsci-2582-4333-4(5)-123

10. Hernandez Bronchud M. Immunomodulatory pathways in both breast cancer and placental tissues: Insights from a unique clinical and genomic case report. JCO. 2017;35:13-13. CrossRef
11. Dunn GP, Bruce AT, Ikeda H, Old LJ, Schreiber RD. Cancer immunoediting: from immunosurveillance to tumor escape. Nat Immunol. 2002;3(11):991-8. PubMed | CrossRef
12. Dunn GP, Old LJ, Schreiber RD. The immunobiology of cancer immunosurveillance and immunoediting. Immunity. 2004;21(2):137-48. PubMed | CrossRef
13. Dunn GP, Old LJ, Schreiber RD. The three Es of cancer immunoediting. Annu Rev Immunol. 2004;22:329-60. PubMed | CrossRef
14. Vinay DS, Ryan EP, Pawelec G, Talib WH, Stagg J, Elkord E, et al. Immune evasion in cancer: Mechanistic basis and therapeutic strategies. InSeminars in Cancer Biology. Academic Press. 2015;35:S185-98. PubMed | CrossRef
15. De Visser KE, Eichten A, Coussens LM. Paradoxical roles of the immune system during cancer development. Nat Rev Cancer. 2006;6(1):24-37. PubMed | CrossRef
16. Zaidi N, Jaffee EM. Immunotherapy transforms cancer treatment. J Clin Invest. 2019;129(1):46-7. PubMed | CrossRef
17. Leach DR, Krummel MF, Allison JP. Enhancement of antitumor immunity by CTLA-4 blockade. Science. 1996;271(5256):1734-6. PubMed | CrossRef
18. Freeman GJ, Long AJ, Iwai Y, Bourque K, Chernova T, Nishimura H, et al. Engagement of the PD-1 immunoinhibitory receptor by a novel B7 family member leads to negative regulation of lymphocyte activation. J Exp Med. 2000;192(7):1027-34. PubMed | CrossRef
19. Iwai Y, Ishida M, Tanaka Y, Okazaki T, Honjo T, Minato N. Involvement of PD-L1 on tumor cells in the escape from host immune system and tumor immunotherapy by PD-L1 blockade. Proc Natl Acad Sci. 2002;99(19):12293-7. PubMed | CrossRef
20. Topalian SL, Drake CG, Pardoll DM. Immune checkpoint blockade: a common denominator approach to cancer therapy. Cancer Cell. 2015;27(4):450-61. PubMed | CrossRef
21. Pardoll DM. The blockade of immune checkpoints in cancer immunotherapy. Nat Rev Cancer. 2012;12(4):252-64. PubMed | CrossRef
22. Diesendruck Y, Benhar I. Novel immune check point inhibiting antibodies in cancer therapy-Opportunities and challenges. Drug Resist Updat. 2017;30:39-47. PubMed | CrossRef
23. Carosella ED, Rouas-Freiss N, Tronik-Le Roux D, Moreau P, LeMaoult J. HLA-G: an immune checkpoint molecule. Adv Immunol. 2015;127:33-144. PubMed | CrossRef
24. Rouas-Freiss N, LeMaoult J, Verine J, Tronik-Le Roux D, Culine S, Hennequin C, et al. Intratumor heterogeneity of immune checkpoints in primary renal cell cancer: focus on HLA-G/ILT2/ILT4. Oncoimmunology. 2017;6(9):e1342023. PubMed | CrossRef
25. RodrÍguez E, Schetters ST, van Kooyk Y. The tumour glyco-code as a novel immune checkpoint for immunotherapy. Nat Rev Immunol. 2018;18(3):204-11. PubMed | CrossRef
26. Holets LM, Hunt JS, Petroff MG. Trophoblast CD274 (B7-H1) is differentially expressed across gestation: influence of oxygen concentration. Biol Reprod. 2006;74(2):352-8. PubMed | CrossRef
27. Enninga EA, Harrington SM, Creedon DJ, Ruano R, Markovic SN, Dong H, et al. Immune checkpoint molecules soluble program death ligand 1 and galectin-9 are increased in pregnancy. Am J Reprod Immunol. 2018;79(2):e12795. PubMed | CrossRef
28. Kshirsagar SK, Alam SM, Jasti S, Hodes H, Nauser T, Gilliam M, et al. Immunomodulatory molecules are released from the first trimester and term placenta via exosomes. Placenta. 2012;33(12):982-90. PubMed | CrossRef
29. Taglauer ES, Trikhacheva AS, Slusser JG, Petroff MG. Expression and function of PDCD1 at the human maternal-fetal interface. Biol Reprod. 2008;79(3):562-9. PubMed | CrossRef
30. Guleria I, Khosroshahi A, Ansari MJ, Habicht A, Azuma M, Yagita H, et al. A critical role for the programmed death ligand 1 in fetomaternal tolerance. J Exp Med. 2005;202(2):231-7. PubMed | CrossRef
31. Yabe S, Alexenko AP, Amita M, Yang Y, Schust DJ, Sadovsky Y, et al. Comparison of Syncytiotrophoblast Generated from Human Embryonic Stem Cells and from Term Placentas. Proc Natl Acad Sci U S A. 2016;113(19):E2598-607. PubMed | CrossRef

Citation: Hernández-Bronchud M. Redeployment of Placental Gene Programming: Can Invasive Placentation Molecular Switches Complement the Hallmarks of Cancer?. J Clin Med Res. 2022;4(5):1-9.
DOI: https://doi.org/10.37191/Mapsci-2582-4333-4(5)-123

32. Okae H, Toh H, Sato T, Hiura H, Takahashi S, Shirane K, et al. Derivation of Human Trophoblast Stem Cells. Cell Stem Cell. 2018;22(1):50-63. PubMed | CrossRef
33. Lavialle C, Cornelis G, Dupressoir A, Esnault C, Heidmann O, Vernochet C, et al. Paleovirology of 'Syncytins', Retroviral Env Genes Exapted For A Role in Placentation. Philos Trans R Soc Lond B Biol Sci. 2013;368(1626):20120507. PubMed | CrossRef
34. D'Souza AW, Wagner GP. Malignant Cancer and Invasive Placentation: A Case for Positive Pleiotropy Between Endometrial and Malignancy Phenotypes. Evol Med Public Health. 2014;2014(1):136-45. PubMed | CrossRef
35. Lala PK, Nandi P, Hadi A, Halari C. A Crossroad Between Placental and Tumor Biology: What Have We Learnt?. Placenta. 2021;116:12-30. PubMed | CrossRef
36. Jung SH, Choi YJ, Kim MS, Park HC, Han MR, Hur SY, et al. Distinct Genomic Profiles of Gestational Choriocarcinoma, A Unique Cancer of Pregnant Tissues. Exp Mol Med.2020;52(12):2046-54. PubMed | CrossRef
37. Roetman JJ, Apostolova MK, Philip M. Viral and Cellular Oncogenes Promote Immune Evasion. Oncogene. 2022;41(7):921-9. PubMed | CrossRef
38. Papuchova H, Latos PA. Transcription Factor Networks in Trophoblast Development. Cell Mol Life Sci. 2022;79(6):1-7. PubMed | CrossRef
39. Hossain SM, Lynch-Sutherland CF, Chatterjee A, Macaulay EC, Eccles MR. Can Immune Suppression and Epigenome Regulation in Placenta offer Novel Insights into Cancer Immune Evasion And Immunotherapy Resistance?. Epigenomes. 2021;5(3):16. PubMed | CrossRef
40. Nordor AV, Nehar-Belaid D, Richon S, Klatzmann D, Bellet D, Dangles-Marie V, et al. The Early Pregnancy Placenta Foreshadows DNA Methylation Alterations of Solid Tumors. Epigenetics. 2017;12(9):793-803. PubMed | CrossRef
41. Jang HS, Shah NM, Du AY, Dailey ZZ, Pehrsson EC, Godoy PM, et al. Transposable Elements Drive Widespread Expression of Oncogenes in Human Cancers. Nat Genet. 2019;51(4):611-7. PubMed | CrossRef
42. Chuong EB, Rumi MA, Soares MJ, Baker JC. Endogenous Retroviruses Function as Species-Specific Enhancer Elements in the Placenta. Nat Genet. 2013;45(3):325-9. PubMed | CrossRef
43. Lynch-Sutherland CF, Chatterjee A, Stockwell PA, Eccles MR, Macaulay EC. Reawakening the Developmental Origins of Cancer Through Transposable Elements. Front Oncol. 2020;10:468. PubMed | CrossRef
44. Illsley NP, Dasilva-Arnold SC, Zamudio S, Alvarez M, Al-Khan A. Trophoblast Invasion: Lessons from Abnormally Invasive Placenta (Placenta Accreta). Placenta. 2020;102:61-6. PubMed | CrossRef
45. Suryawanshi H, Morozov P, Straus A, Sahasrabudhe N, Max KE, Garzia A, et al. A Single-Cell Survey of the Human First-Trimester Placenta and Decidua. Sci Adv. 2018;4(10):eaau4788. PubMed | CrossRef
46. Huang JY, Yu PH, Li YC, Kuo PL. NLRP7 Contributes To in Vitro Decidualization of Endometrial Stromal Cells. Reprod Biol Endocrinol. 2017;15(1):1-0. PubMed | CrossRef
47. Meissner TB, Li A, Biswas A, Lee KH, Liu YJ, Bayir E, et al. NLR Family Member NLRC5 Is A Transcriptional Regulator of MHC Class I Genes. Proc Natl Acad Sci U S A. 2010;107(31):13794-9. PubMed | CrossRef
48. Bruchard M, Rebé C, Derangère V, Togbé D, Ryffel B, Boidot R, et al. The Receptor NLRP3 is a Transcriptional Regulator of TH2 Differentiation. Nat Immunol. 2015;16(8):859-70. PubMed | CrossRef
49. Singer H, Biswas A, Nuesgen N, Oldenburg J, El-Maarri O. NLRP7, Involved in Hydatidiform Molar Pregnancy (HYDM1), Interacts with the Transcriptional Repressor ZBTB16. PL0S One. 2015;10(6):e0130416. PubMed | CrossRef

Citation: Hernández-Bronchud M. Redeployment of Placental Gene Programming: Can Invasive Placentation Molecular Switches Complement the Hallmarks of Cancer?. J Clin Med Res. 2022;4(5):1-9.
DOI: https://doi.org/10.37191/Mapsci-2582-4333-4(5)-123