# Review of: "Introduction to Evolutionary Cancer Cell Biology (ECCB) and Ancestral Cancer Genomics"

Konieczny Leszek[1]

1 Akademickie Centrum Komputerowe CYFRONET AGH

Potential competing interests: No potential competing interests to declare.

A gigantic development of analytical techniques concerning DNA and RNA opens the door to understanding molecular biology and makes also natural the expectation of breaking cancer mistery finally. Unfortunately cancerogenesis still remains largerly enigmatic.

The initiation of cancer disease is generally correlated with the increased mutability caused by direct action of cancerogenic factors on DNA or indirectly by overstimulation of cell proliferation. Excessive cell proliferation causes disturbance in chromatin organisation and unproper DNA packing. Mutations are the result. Many different mutations preceede and associate usually cancerogenic process. Some of them are certainly those searched by scientists. However sets of mutated genes in different cases do not overlap entirely and enigma remains.

Different ideas were supplied to explain cancerogenesis. Attractive seems the one which assumes the appearance of specific cancerogenic genome early in precambrian period. According to the idea this construct of genes still exists in our genomes initiating cancer transformation when awaken. In such case however different cancers should reveal similar sets of genetic cancer drivers. Unfortunately the observed mutated genes combinations found in different cancers do not seem to reveal the suggested common model of cancer driving genes.

Besides surviving for such long time of destructive genome favoring elimination of species during evolution seems rather doubtful.

Two critical areas of cell activity must have been occupied by new sets of genes when organisms were created in evolution. These were: specialisation (*epigenetics*) and subordination (*contact inhibition, apoptosis, suppressor genes, senescence* and others). Defective action of genes in these areas may start cancer transformation. However sets of cancer driving genes may not be identical.

It is likely that different sets of mutated genes ensuring chromatin stability initiate cancer. Interpretation is additionaly complicated because many randomly generated secondary mutations which associate cancer cell proliferation may pretend to be cancer drivers.

Although the knowledge of cancerogenesis proceedes, it is still on the debatable level. It seems that we must wait yet for some years before the final definition concerning cancerogenesis will appear.

Drost J, van Jaarsveld RH, Ponsioen B, Zimberlin C, van Boxtel R, Buijs A, Sachs N, Overmeer RM, Offerhaus GJ,

Begthel H, Korving J, van de Wetering M, Schwank G, Logtenberg M, Cuppen E, Snippert HJ, Medema JP, Kops GJ, Clevers H. Sequential cancer mutations in cultured human intestinal stem cells. Nature. 2015 ; 521(7550):43-7. doi: 10.1038/nature14415.

Kandoth C, McLellan MD, Vandin F, Ye K, Niu B, Lu C, Xie M, Zhang Q, McMichael JF, Wyczalkowski MA, Leiserson MDM, Miller CA, Welch JS, Walter MJ, Wendl MC, Ley TJ, Wilson RK, Raphael BJ, Ding L. Mutational landscape and significance across 12 major cancer types. Nature. 2013 ; 502(7471):333-339. doi: 10.1038/nature12634

Liu Y, Chen C, Xu Z, Scuoppo C, Rillahan CD, Gao J, Spitzer B, Bosbach B, Kastenhuber ER, Baslan T, Ackermann S, Cheng L, Wang Q, Niu T, Schultz N, Levine RL, Mills AA, Lowe SW. Deletions linked to TP53 loss drive cancer through p53-independent mechanisms. Nature. 2016 ; 531(7595):471-475. doi: 10.1038/nature17157.

Vogelstein B, Papadopoulos N, Velculescu VE, Zhou S, Diaz LA Jr, Kinzler KWCancer genome landscapes. Science. 2013 ; 339(6127):1546-58. doi: 10.1126/science.1235122

Terekhanova NV, Karpova A, Liang WW, Strzalkowski A, Chen S, Li Y, Southard-Smith AN, Iglesia MD, Wendl MC, Jayasinghe RG, Liu J, Song Y, Cao S, Houston A, Liu X, Wyczalkowski MA, Lu RJ, Caravan W, Shinkle A, Naser Al Deen N, Herndon JM, Mudd J, Ma C, Sarkar H, Sato K, Ibrahim OM, Mo CK, Chasnoff SE, Porta-Pardo E, Held JM, Pachynski R, Schwarz JK, Gillanders WE, Kim AH, Vij R, DiPersio JF, Puram SV, Chheda MG, Fuh KC, DeNardo DG, Fields RC, Chen F, Raphael BJ, Ding L. Epigenetic regulation during cancer transitions across 11 tumour types. Nature. 2023 ; 623(7986):432-441. doi: 10.1038/s41586-023-06682-5.

Tang J, Fewings E, Chang D, Zeng H, Liu S, Jorapur A, Belote RL, McNeal AS, Tan TM, Yeh I, Arron ST, Judson-Torres RL, Bastian BC, Shain AH. The genomic landscapes of individual melanocytes from human skin. Nature. 2020 ; 586(7830):600-605. doi: 10.1038/s41586-020-2785-8.

Kim M, Park J, Bouhaddou M, Kim K, Rojc A, Modak M, Soucheray M, McGregor MJ, O'Leary P, Wolf D, Stevenson E, Foo TK, Mitchell D, Herrington KA, Muñoz DP, Tutuncuoglu B, Chen KH, Zheng F, Kreisberg JF, Diolaiti ME, Gordan JD, Coppé JP, Swaney DL, Xia B, van 't Veer L, Ashworth A, Ideker T, Krogan NJ. A protein interaction landscape of breast cancer. Science. 2021 ; 374(6563):eabf3066. doi: 10.1126/science.abf3066.

Zheng F, Kelly MR, Ramms DJ, Heintschel ML, Tao K, Tutuncuoglu B, Lee JJ, Ono K, Foussard H, Chen M, Herrington KA, Silva E, Liu SN, Chen J, Churas C, Wilson N, Kratz A, Pillich RT, Patel DN, Park J, Kuenzi B, Yu MK, Licon K, Pratt D, Kreisberg JF, Kim M, Swaney DL, Nan X, Fraley SI, Gutkind JS, Krogan NJ, Ideker T. Interpretation of cancer mutations using a multiscale map of protein systems. Science. 2021 ; 374(6563):eabf3067. doi: 10.1126/science.abf3067.

Williams N, Lee J, Mitchell E, Moore L, Baxter EJ, Hewinson J, Dawson KJ, Menzies A, Godfrey AL, Green AR, Campbell PJ, Nangalia J. Life histories of myeloproliferative neoplasms inferred from phylogenies. Nature. 2022 ; 602(7895):162-168. doi: 10.1038/s41586-021-04312-6.

Madan E, Pelham CJ, Nagane M, Parker TM, Marques R, Fazio K, Shaik K, Yuan Y, Henriques V, Galzerano

A, Yamashita T, Ferreira Pinto MA, Palma AM, Camacho D, Vieira A, Soldini D, Nakshatri H, Post SR, Rhiner C, Yamashita H, Accardi D, Hansen LA, Carvalho C, Beltran AL, Kuppusamy P, Gogna R, Moreno E. Flower isoforms promote competitive growth in cancer. Nature. 2019 , 572(7768):260-264. doi: 10.1038/s41586-019-1429-3.

Filbin MG, Tirosh I, Hovestadt V, Shaw ML, Escalante LE, Mathewson ND, Neftel C, Frank N, Pelton K, Hebert CM, Haberler C, Yizhak K, Gojo J, Egervari K, Mount C, van Galen P, Bonal DM, Nguyen QD, Beck A, Sinai C, Czech T, Dorfer C, Goumnerova L, Lavarino C, Carcaboso AM, Mora J, Mylvaganam R, Luo CC, Peyrl A, Popović M, Azizi A, Batchelor TT, Frosch MP, Martinez-Lage M, Kieran MW, Bandopadhayay P, Beroukhim R, Fritsch G, Getz G, Rozenblatt-Rosen O, Wucherpfennig KW, Louis DN, Monje M, Slavc I, Ligon KL, Golub TR, Regev A, Bernstein BE, Suvà ML. Developmental and oncogenic programs in H3K27M gliomas dissected by single-cell RNA-seq.Science. 2018 ; 360(6386):331-335. doi: 10.1126/science.aao4750.

Bick AG et al. Inherited causes of clonal haematopoiesis in 97,691 whole genomes. Nature. 2020; 586(7831):763-768. doi: 10.1038/s41586-020-2819-2.

Trigos AS, Pearson RB, Papenfuss AT, Goode DL. Altered interactions between unicellular and multicellular genes drive hallmarks of transformation in a diverse range of solid tumors. Proc Natl Acad Sci U S A. 2017; 114(24):6406-6411. doi: 10.1073/pnas.1617743114.

Niculescu VF. Introduction to evolutionary cancer cell biology (ECCB) and ancestal cancer genomics.

Niculescu VF.On t he role of polyploid giant cells in oncogenesis and tumorigenesisMed Oncol. 2023 ; 40(8):232. doi: 10.1007/s12032-023-02089-4.