Clonal interference of signaling mutations worsens prognosis in core-binding factor acute myeloid leukemia.

Titre	Clonal interference of signaling mutations worsens prognosis in core-binding factor acute myeloid leukemia.
Type de publication	Article de revue
Auteur	Itzykson, Raphael [1], Duployez, Nicolas [2], Fasan, Annette [3], Decool, Gauthier [4], Marceau-Renaut, Alice [5], Meggendorfer, Manja [6], Jourdan, Eric [7], Petit, Arnaud [8], Lapillonne, Hélène [9], Micol, Jean-Baptiste [10], Cornillet-Lefèbvre, Pascale [11], Ifrah, Norbert [12], Leverger, Guy [13], Dombret, Hervé [14], Boissel, Nicolas [15], Haferlach, Torsten [16], Preudhomme, Claude [17]
Editeur	American Society of Hematology
Type	Article scientifique dans une revue à comité de lecture
Année	2018
Langue	Anglais
Date	2018 Jul 12
Pagination	187-196
Volume	132
Titre de la revue	Blood
ISSN	1528-0020
Résumé en anglais	Mutations in receptor tyrosine kinase/RAS signaling pathway genes are frequent in core-binding factor (CBF) acute myeloid leukemias (AMLs), but their prognostic relevance is debated. A subset of CBF AML patients harbors several signaling gene mutations. Genotyping of colonies and of relapse samples indicates that these arise in independent clones, thus defining a process of clonal interference (or parallel evolution). Clonal interference is pervasive in cancers, but the mechanisms underlying this process remain unclear, and its prognostic impact remains unknown. We analyzed a cohort of 445 adult and pediatric patients with CBF AML treated with intensive chemotherapy and with deep sequencing of 6 signaling genes (, , , , ,). A total of 152 (34%), 167 (38%), and 126 (28%) patients harbored no, a single, and multiple signaling clones (clonal interference), respectively. Clonal interference of signaling mutations was associated with older age (= .004) and inv(16) subtype (= .025) but not with white blood cell count or mutations in chromatin or cohesin genes. The median allele frequency of signaling mutations was 31% in patients with a single clone or clonal interference (= .14). The repertoire of , , and / variants differed between groups. Clonal interference did not affect complete remission rate or minimal residual disease after 1-2 courses, but it did convey inferior event-free survival (< 10), whereas the presence of a single signaling clone did not (= .44). This inferior outcome was independent of clinical parameters and of the presence of specific signaling clones. Our results suggest that specific clonal architectures can herald distinct prognoses in AML.
URL de la notice	http://okina.univ-angers.fr/publications/ua18762 [18]

DOI	10.1182/blood-2018-03-837781 [19]
Autre titre	Blood
Identifiant (ID) PubMed	29692343 [20]

Liens
[1] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=33564
[2] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=33565
[3] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=33566
[4] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=33567
[5] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=33568
[6] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=33569
[7] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=30327
[8] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=33570
[9] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=33571
[10] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=33572
[11] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=16430
[12] http://okina.univ-angers.fr/no.ifrah/publications
[13] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=32532
[14] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=32975
[15] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=32963
[16] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=33573
[17] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=33494
[18] http://okina.univ-angers.fr/publications/ua18762
[19] http://dx.doi.org/10.1182/blood-2018-03-837781
[20] http://www.ncbi.nlm.nih.gov/pubmed/29692343?dopt=Abstract