Nuclear factor erythroid 2-related factor 2 nuclear translocation induces myofibroblastic dedifferentiation in idiopathic pulmonary fibrosis

Titre	Nuclear factor erythroid 2-related factor 2 nuclear translocation induces myofibroblastic dedifferentiation in idiopathic pulmonary fibrosis
Type de publication	Article de revue
Auteur	Artaud-Macari, Elise [1], Goven, Delphine [2], Brayer, Stéphanie [3], Hamimi, Akila [4], Besnard, Valérie [5], Marchal-Sommé, Joëlle [6], El Ali, Zeina [7], Crestani, Bruno [8], Kerdine-Römer, Saadia [9], Boutten, Anne [10], Bonay, Marcel [11]
Editeur	Mary Ann Liebert
Type	Article scientifique dans une revue à comité de lecture
Année	2013
Langue	Anglais
Date	1er Janv. 2013
Numéro	1
Pagination	66-79
Volume	18
Titre de la revue	Antioxidants & redox signaling
ISSN	1557-7716
Mots-clés	Active Transport, Cell Nucleus [12], Aldehydes [13], Animals [14], Cell Dedifferentiation [15], Cell Nucleus [16], Cells, Cultured [17], Collagen Type I [18], Epoxide Hydrolases [19], Gene Knockdown Techniques [20], Heme Oxygenase-1 [21], Humans [22], Idiopathic Pulmonary Fibrosis [23], Isothiocyanates [24], Lipid Peroxidation [25], Male [26], Mice [27], Mice, Inbred C57BL [28], Mice, Knockout [29], Myofibroblasts [30], NAD(P)H Dehydrogenase (Quinone) [31], NF-E2-Related Factor 2 [32], Oxidative Stress [33], Phenotype [34], Proto-Oncogene Proteins c-sis [35], RNA, Small Interfering [36], Thiocyanates [37], Transforming Growth Factor beta [38]

Résumé en anglais	AIMS: Oxidants have been implicated in the pathophysiology of idiopathic pulmonary fibrosis (IPF), especially in myofibroblastic differentiation. We aimed at testing the hypothesis that nuclear factor erythroid 2-related factor 2 (Nrf2), the main regulator of endogenous antioxidant enzymes, is involved in fibrogenesis via myofibroblastic differentiation. Fibroblasts were cultured from the lungs of eight controls and eight IPF patients. Oxidants-antioxidants balance, nuclear Nrf2 expression, and fibroblast phenotype (α-smooth muscle actin and collagen I expression, proliferation, migration, and contraction) were studied under basal conditions and after Nrf2 knockdown or activation by Nrf2 or Keap1 siRNA transfection. The effects of sulforaphane (SFN), an Nrf2 activator, on the fibroblast phenotype were tested under basal and pro-fibrosis conditions (transforming growth factor β [TGF-β]). RESULTS: Decreased Nrf2 expression was associated with a myofibroblast phenotype in IPF compared with control fibroblasts. Nrf2 knockdown induced oxidative stress and myofibroblastic differentiation in control fibroblasts. Conversely, Nrf2 activation increased antioxidant defences and myofibroblastic dedifferentation in IPF fibroblasts. SFN treatment decreased oxidants, and induced Nrf2 expression, antioxidants, and myofibroblastic dedifferentiation in IPF fibroblasts. SFN inhibited TGF-β profibrotic deleterious effects in IPF and control fibroblasts and restored antioxidant defences. Nrf2 knockdown abolished SFN antifibrosis effects, suggesting that they were Nrf2 mediated. INNOVATION AND CONCLUSION: Our findings confirm that decreased nuclear Nrf2 plays a role in myofibroblastic differentiation and that SFN induces human pulmonary fibroblast dedifferentiation in vitro via Nrf2 activation. Thus, Nrf2 could be a novel therapeutic target in IPF.
URL de la notice	http://okina.univ-angers.fr/publications/ua16152 [39]
DOI	10.1089/ars.2011.4240 [40]
Lien vers le document	http://online.liebertpub.com/doi/abs/10.1089/ars.2011.4240 [41]
Titre abrégé	Antioxid. Redox Signal.
Identifiant (ID) PubMed	22703534 [42]

Liens

[1] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=27046
[2] http://okina.univ-angers.fr/delphine.goven/publications
[3] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=27047
[4] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=27048
[5] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=27049
[6] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=11520
[7] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=27050
[8] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=27051
[9] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=27052
[10] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=11518
[11] http://okina.univ-angers.fr/publications?f%5Bauthor%5D=11523
[12] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=23313
[13] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=19199
[14] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=964
[15] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=23314
[16] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=7479
[17] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=1428

[18] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=23315
[19] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=23316
[20] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=23317
[21] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=11641
[22] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=991
[23] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=23318
[24] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=17859
[25] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=8459
[26] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=968
[27] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=1102
[28] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=1478
[29] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=1147
[30] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=8334
[31] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=23319
[32] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=11643
[33] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=6203
[34] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=1491
[35] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=23320
[36] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=10781
[37] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=23321
[38] http://okina.univ-angers.fr/publications?f%5Bkeyword%5D=23322
[39] http://okina.univ-angers.fr/publications/ua16152
[40] http://dx.doi.org/10.1089/ars.2011.4240
[41] http://online.liebertpub.com/doi/abs/10.1089/ars.2011.4240
[42] http://www.ncbi.nlm.nih.gov/pubmed/22703534?dopt=Abstract