Journal of Umm Al-Qura University for Medical Sciences

Journal homepage: https://uqu.edu.sa/en/mj

Case Report

DOCK8 Deficiency Presenting with Progressive Multifocal Leukoencephalopathy: A Case Report

*Abeer Tamnqani [1], Aisha Mirza[2], Husni Rayes[2], Amer Khojah[3]**

1 College of Medicine, Umm Al-Qura University, Makkah 21955, Saudi Arabia

2 Makkah Maternity and Children Hospital, Makkah, Saudi Arabia.

3 Department of Pediatrics, College of Medicine, Umm Al-Qura University, Makkah 21955, Saudi Arabia

ARTICLE INFO

Received: 20/09/2024
Accepted: 17/02/2025

Keywords:
DOCK8; PML; primary immunodeficiencies; Central nervous system; hyperimmunoglobulin E syndrome

***Corresponding author:**
Amer Khojah, MD
E:amkhojah@uqu.edu.sa

ABSTRACT

1) Background: Dedicator of cytokinesis 8 (DOCK8) deficiency is a rare autosomal recessive form of hyperimmunoglobulin E syndrome characterized by autoimmunity, atopy, recurrent infections, and increased malignancy risk. Neurological manifestations, including central nerv-ous system (CNS) vasculitis and stroke, have been documented, but progressive multifocal leukoencephalopathy (PML) remains a rare complication.

(2) Case Report: We present the case of a 27-month-old female from a consanguineous family who presented to the hospital with developmental regression and seizures, and was diagnosed with progressive multifocal leukoencephalopathy (PML). Laboratory evaluation revealed thrombocytosis, elevated inflammatory markers, and a markedly elevated serum IgE level of 1783.5 IU/ml (normal range: ≤ 15 IU/ml). Whole-exome sequencing identified a homozygous mutation in the DOCK8 gene, affecting the splice site in intron 15 (c.1797+1G>T). Despite extensive supportive treatments, including intravenous immunoglobulin and antimicrobial prophylaxis, the patient's condition continued to worsen. She is currently undergoing evaluation for hematopoietic stem cell transplantation (HSCT).

(3) Conclusion: This case highlights progressive multifocal leukoencephalopathy (PML) as a rare but severe neurological complication of DOCK8 deficiency. Early recognition and treat-ment of DOCK8 deficiency are of paramount importance, as delays in diagnosis can result in severe complications, as demonstrated in our patient.

INTRODUCTION

Dedicator of cytokinesis 8 (DOCK 8) deficiency (OMIM#611432), a rare autosomal recessive form of hyper-immunoglobulin E (IgE), was first described in 2008 (Griggs, Ladd, Saul, DuPont, & Srivastava, 2008). It is more prevalent in populations with increased con-sanguinity rates, such as in regions like Saudi Arabia, where consanguineous marriages occur in 56% of cases (Khayat et al., 2024). DOCK8 deficiency results in many immune system abnormalities, including im-paired cell migration, dysfunctional T-cell activity and impaired antigen-specific antibody production (Biggs, Keles, & Chatila, 2017; M. Zhang et al., 2024). These abnormalities lead to a variety of clinical features such as autoimmunity, atopy such as asthma, skin eczema, and recurrent infections as well as persistent viral and candidal infections (Biggs et al., 2017; Ganesan et al., 2024; Liquidano-Perez et al., 2024; Singh et al., 2024). Additionally, there is an increased risk of malignancy including lymphoma and squamous cell carcinomas in patients with DOCK8 deficiency (Susanne E. Aydin et al., 2015; Kumar Jindal et al., 2024). Hematopoietic stem cell transplantation has been utilized as a treat-ment for DOCK8 deficiency (Freeman et al., 2025).

Although central nervous system (CNS) vasculitis and strock are well documented in patients with DOCK8 deficiency (AlKhater, 2016; Susanne E. Aydin et al., 2015; Biggs et al., 2017; Boztug et al., 2012; Liquidano-Pérez et al., 2022), other CNS abnormalities, including neurodevelopmental disorder, moyamoya disease, en-cephalopathy, and viral encephalitis have been sporad-ically reported (Alsum et al., 2013; Susanne E. Aydin et al., 2015; K. R. Engelhardt et al., 2009; Ibrahim et al., 2023; Krgovic, Kokalj Vokac, Zagorac, & Gregoric Kumperscak, 2018). CNS involvement can significantly impair the quality of life and lead to premature mortali-ty (Kose,

DOI: https://doi.org/10.54940/ms43585950

Karali, Bodur, Cekic, & Kilic, 2024; Yildirim et al., 2018). Early recognition of neurological involve-ment may provide a window for intervention before permanent neurological damage occurs. Herein, we re-port a case of DOCK8 deficiency in a female toddler who presented with progressive multifocal leu-koencephalopathy.

2. CASE PRESENTATION

A 27-month-old full-term girl, born to consanguineous parents, was referred to our pediatric intensive care unit (PICU) with a two-week history of fever and cough. Initially, she was diagnosed with pneumonia at a referring hospital and was treated with ceftriaxone and azithromycin. Despite antibiotic treatment, her symptoms persisted. On day five of admission her level of consciousness gradually worsened, and she experienced multiple episodes of seizures, necessitating antiepileptic treatment with levetiracetam. Subsequently, she required PICU admission due to a disturbed level of consciousness and the need for ventilatory support.

Her family reported a history of recurrent pneumonia since infancy and observed a decline in developmental skills over the past two months. Upon presentation to our PICU, she was on mechanical ventilation, with a temperature of 38.9 °C, BP 102/89 mmHg, and pulse was 100 bpm. She was sedated, non-dysmorphic, and no abnormalities were noted in her nails, skin, or joints. In addition, there were no signs of organomegaly or lymphadenopathy.

A blood workup revealed leukocytosis (WBC 18.6 x 10^3/μL) with a differential count of neutrophils 12.4 x 10^3/μL, lymphocytes 2.88 x 10^3/μL, monocytes 2.19 x 10^3/μL, and eosinophils 1.08 x 10^3/μL. Anemia (HB 9.5 g/dL) and thrombocytosis (Platelets 705 x 10^3/μL) were also noted. The ESR was 40 mm/h, and CRP was 4.9 mg/dL. Ammonia and lactate levels were within normal limits, as were other chemistry tests. Blood and urine cultures were negative, HIV PCR was negative, and the newborn screening was normal. The CSF analysis revealed a cell count of zero, with normal CSF glucose and protein levels, and the CSF culture showed no growth. The serum IgE level was markedly elevated at 1783.5 IU/ml (normal range: ≤ 15 IU/ml), Chest radiography revealed pneumonic infiltrate in the right and left upper lobe. A brain MRI showed diffusion restriction in the right temporoparietal, right insular, and left fronto-temporo-parietal regions, as well as chronic and subacute insults with atrophic changes, and bilateral asymmetric cerebral encephalopathy suggestive of progressive multifocal leukoencephalopathy (Figure 1). The electroencephalogram (EEG) result was normal.

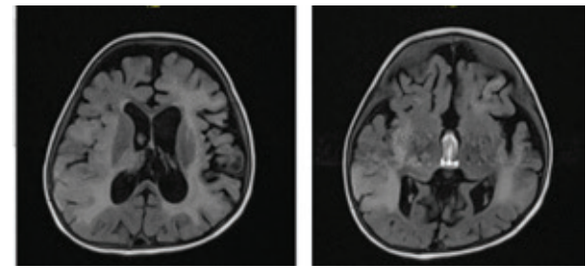

Figure 1. Brain MRI showing possible mitochondrial encephalomyopathy. Abnormal generalized periventricular T2 hyperintensity. There is volume loss, leading to the enlargement of both the lateral and third ventricles.

Given the clinical presentation, hyperimmunoglobulin E syndrome (HIES) was suspected. Whole-exome sequences (WES) showed a novel pathogenic homozygous mutation in the DOCK8 gene, affecting the splice site in intron 15 c.1797+1G>T. The patient's 6-year-old elder sister, who presented with an -Eczema-like rash, underwent genetic testing and was found to have the same DOCK8 mutation. Both patients were initiated on intravenous immunoglobulin therapy, sulfamethoxazole and trimethoprim, and fluconazole prophylaxis by the immunologist, and referred to a transplant center for consideration of bone marrow transplant.

3. DISCUSSION

DOCK8 belongs to the DOCK180 superfamily which plays a crucial role in immune cell function (Ruusala & Aspenström, 2004; Q. Zhang et al., 2009). DOCK8 is involved in regulating cytoskeletal rearrangements, which are crucial for maintaining cellular structure, enabling migration, and facilitating adhesion. Furthermore, research has linked DOCK8 to various aspects of immune function, including CD4+ T-cell differentiation, immune synapse formation, and processes related to tumor immunity such as immune cell infiltration into tumors (Lambe et al., 2011; L. Zhang, Cao, Dai, & Zhang, 2022). DOCK8 defects impact the immune system, leading to combined immunodeficiency, characterized by impaired T-cell function in addition to dysfunctional B-cells and natural killer cells (Q. Zhang et al., 2009). Patients typically have low absolute counts of both CD4+ and CD8+ T cells, diminished cell proliferation, and reduced production of the antiviral cytokines IFN-γ and TNF-α, which contribute to susceptibility to viral infections (Crawford et al., 2013; Engelhardt et al., 2015; Lambe et al., 2011; Q. Zhang et al., 2009; Q. Zhang, Jing, & Su, 2016). Additionally, there is a decreased presence of TH17 cells, increasing susceptibility to fungal infections, and TH2 skewing, leading to severe atopy (K. R. Engelhardt et al., 2009; Tangye et al., 2017). Lastly, there are defective antibody responses, especially to polysaccharide antigens, resulting from impaired class switching and affinity maturation,

increasing suscepti-bility to bacterial infections (Engelhardt et al., 2015; Randall, Lambe, Goodnow, & Cornall, 2010; Q. Zhang et al., 2016).

In addition, DOCK8 deficiency has been associated with a small number of patients presenting with severe central nervous system (CNS) lesions. manifesting as hemiplegia, seizures, ischemic infarction, subarachnoid hemorrhage, central nervous system vasculitis combined with stroke, facial paralysis, and viral encephalitis(AlKhater, 2016; Alsum et al., 2013; Susanne E. Aydin et al., 2015; Biggs et al., 2017; K. R. Engelhardt et al., 2009; Ibrahim et al., 2023; Krgovic et al., 2018; J. Yang & Y. Liu, 2021). A study involving 20 families, reported neurological symptoms in 10 patients, including meningitis, CNS vasculitis, progressive multifocal leukoencephalopathy (PML), and fatal encephalitis (K. R. Engelhardt et al., 2009). In another study of 25 patients, five individuals presented with neurological symptoms such as hemiparesis and sei-zures. Neuroimaging revealed Moyamoya disease in one patient, middle cerebral artery syndrome in another, and brain infarctions in the remaining three patients (Alsum et al., 2013).

Progressive multifocal leukoencephalopathy (PML) is a rare, severe, and potentially fatal viral brain infection that is primarily observed in immunocompromised pa-tients, such as those with DOCK8. (Hadjadj et al., 2019). The primary causative agent is the polyomavirus JC virus (Cortese, Reich, & Nath, 2021; Ferenczy et al., 2012) which targets oligodendrocytes, crosses the blood-brain barrier, and causes widespread demyelination in the cerebral and cerebellar hemispheres, as observed in the patient's brain MRI, which showed bilateral asymmetric cerebral encephalopathy. progressing insidiously over weeks to months (Cortese et al., 2021). Clinically, PML often manifests with focal symptoms such as hemiparesis, visual deficits, aphasia, ataxia, personality changes, cognitive decline, speech abnormalities, and new-onset seizures. Its multifocal nature affects various brain regions, predominantly the posterior regions, including the brain stem, cerebellum, and occipital lobe, which influence the clinical symptoms (Ferenczy et al., 2012).

Hematopoietic stem cell transplantation (HSCT) re-mains the most effective treatment for patients with DOCK8 deficiency (Susanne E Aydin et al., 2019; Susanne E. Aydin et al., 2015; Cuellar-Rodriguez et al., 2015; Freeman et al., 2025; Pillay et al., 2019). Without intervention, the patient is likely to experience progres-sive deterioration due to recurrent infections and wors-ening PML, ultimately leading to severe neurological decline and increased mortality. While immunoglobulin therapy and antimicrobial prophylaxis may provide temporary infection control, they do not address the underlying immunodeficiency or prevent PML progres-sion.(Hadjadj et al., 2019). In contrast, HSCT offers the potential to restore immune system function, signifi-cantly improving prognosis and reducing the risk of op-portunistic infections like PML. However, the success of HSCT depends on timely intervention to prevent irreversible neurological damage(Susanne E. Aydin et al., 2015). Our patient presented with a novel homozygous loss-of-function (LOF) mutation in the DOCK8 gene, affecting the splice site in intron 15 (c.1797+1G>T). This mutation is predicted to disrupt RNA splicing, leading to aberrant protein synthesis, and resulting in a LOF vari-ant of the DOCK8 protein. Splice-site mutations in DOCK8, such as c.1868+2T>C and c.5962-2A>G, have previously been reported(Jing Yang & Yan Liu, 2021), and are known to impair immune cell function and con-tribute to significant immune dysfunction(Q. Zhang et al., 2009). However, the c.1797+1G>T mutation identi-fied in this case has not been previously documented. Its position at a critical splice donor site likely causes exon 15 skipping or intron retention, ultimately render-ing the DOCK8 protein nonfunctional(Karin R. Engelhardt et al., 2009).

The clinical manifestations in our patient, as well as her sibling, align with the disruption caused by this mutation. The younger sibling presented with progressive multifocal leukoencephalopathy (PML), a rare and severe complication of DOCK8 deficiency, confirmed by brain MRI, which revealed bilateral asymmetric cerebral encephalopathy. Unfortunately, a PCR assay for JC viral DNA in the CSF was not performed due to the lack of availability of the test at our center. Despite suggestive MRI findings and clinical presentation, the absence of confirmation through the PCR assay presents a significant limitation in this case report. Meanwhile, the elder sibling exhibited milder symptoms, such as eczema and recurrent infections, highlighting potential phenotypic variability influenced by environmental factors, additional genetic variations, or differences in the timing of clinical evaluation.

4. CONCLUSION AND RECOMMENDATION

This case report highlights progressive multifocal leu-koencephalopathy (PML) as a rare and severe presenta-tion of DOCK8 deficiency. It emphasizes the necessity of a multidisciplinary approach to the diagnosis and management of DOCK8 deficiency. Early recognition and treatment of DOCK8 deficiency are of paramount importance, as delays in diagnosis can result in severe complications, as demonstrated in our patient.

ABBREVIATIONS

DOCK 8: Dedicator of cytokinesis 8, IgE: Immuno-globulin E, CNS: Central nervous system, PICU: pediat-ric intensive care unit, WBC: White blood cell, Hb: He-moglobin, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, HIV: Human immunodeficiency virus, PCR: Polymerase chain reaction, CSF: cerebro-spinal fluid MRI: Magnetic Resonance Imaging, EEG: Electroencephalogram, HIES: Hyperimmu-

noglobulin E syndrome, WES: Whole Exome Sequencing, PML: Pro-gressive multifocal leukoencephalopathy, JC: John Cunningham virus, HSCT: Hematopoietic stem cell transplantation.

AUTHOR CONTRIBUTION

All authors have read and agreed to the published ver-sion of the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTIC-IPATE

Informed consent was taken from the parents. The study was conducted in accordance with the Declara-tion of Helsinki. Ethical approval was obtained from the Biomedical Research Ethics Committee of Umm AL-Qura University (HAPO-02-K-012-2024-10-2288).

SOURCE OF FUNDING

This research received no external funding

CONFLICT OF INTEREST

The authors declare that they have no competing inter-ests.

ACKNOWLEDGEMENTS

None

REFERENCES

AlKhater, S. A. (2016).
CNS vasculitis and stroke as a complication of DOCK8 deficiency: a case report. BMC Neurol, 16, 54. doi:10.1186/s12883-016-0578-3

Alsum, Z., Hawwari, A., Alsmadi,
O., Al-Hissi, S., Borrero, E., Abu-staiteh, A., . . . Arnaout, R. (2013). Clinical, immunological and molecular characterization of DOCK8 and DOCK8-like deficient patients: single center experience of twenty five patients. Journal of clinical immunology, 33, 55-67.

Aydin, S. E., Freeman,
A. F., Al-Herz, W., Al-Mousa, H. A., Arnaout, R. K., Aydin, R. C., . . . Bredius, R. G. (2019). Hematopoietic stem cell transplantation as treatment for patients with DOCK8 deficiency. The Journal of Allergy and Clinical Immunology: In Practice, 7(3), 848-855.

Aydin, S. E., Kilic, S. S., Aytekin,
C., Kumar, A., Porras, O., Kainulainen, L., . . . On behalf of the inborn errors working party of, E. (2015). DOCK8 Deficiency: Clinical and Immunological Phenotype and Treatment Options - a Review of 136 Patients. Journal of Clinical Immunology, 35(2), 189-198. doi:10.1007/s10875-014-0126-0

Biggs, C. M., Keles,
S., & Chatila, T. A. (2017). DOCK8 deficiency: Insights into pathophysiology, clinical features and management. Clin Immunol, 181, 75-82. doi:10.1016/j.clim.2017.06.003

Boztug, H., Karitnig-Weiß,
C., Ausserer, B., Renner, E. D., Albert, M. H., Sawalle-Belohradsky, J., . . . Matthes-Martin, S. (2012). Clinical and immunological correction of DOCK8 deficiency by allogeneic hematopoietic stem cell transplantation following a reduced toxicity conditioning regimen. Pediatr Hematol Oncol, 29(7), 585-594. doi:10.3109/08880018.2012.714844

Cortese, I., Reich, D. S., & Nath, A. (2021).
Progressive multifocal leukoencephalopathy and the spectrum of JC virus-related disease. Nat Rev Neurol, 17(1), 37-51. doi:10.1038/s41582-020-00427-y

Crawford, G., Enders,
A., Gileadi, U., Stankovic, S., Zhang, Q., Lambe, T., . . . Cornall, R. J. (2013). DOCK8 is critical for the survival and function of NKT cells. Blood, 122(12), 2052-2061. doi:10.1182/blood-2013-02-482331

Cuellar-Rodriguez, J., Freeman,
A. F., Grossman, J., Su, H., Parta, M., Murdock, H., . . . Moutsopoulos, N. (2015). Matched related and unrelated donor hematopoietic stem cell transplantation for DOCK8 deficiency. Biology of Blood and Marrow Transplantation, 21(6), 1037-1045.

Engelhardt, K. R., Gertz,
M. E., Keles, S., Schäffer, A. A., Sigmund, E. C., Glocker, C., . . . Grimbacher, B. (2015). The extended clinical phenotype of 64 patients with dedicator of cytokinesis 8 deficiency. J Allergy Clin Immunol, 136(2), 402-412. doi:10.1016/j.jaci.2014.12.1945

Engelhardt, K. R., McGhee,
S., Winkler, S., Sassi, A., Woellner, C., Lopez-Herrera, G., . . . Chatila, T. A. (2009). Large deletions and point mutations involving the dedicator of cytokinesis 8 (DOCK8) in the autosomal-recessive form of hyper-IgE syndrome. Journal of Allergy and Clinical Immunology, 124(6), 1289-1302.e1284. doi :https://doi.org/10.1016/j.jaci.2009.10.038

Engelhardt, K. R., McGhee,
S., Winkler, S., Sassi, A., Woellner, C., Lopez-Herrera, G., . . . Chatila, T. A. (2009). Large deletions and point mutations involving the dedicator of cytokinesis 8 (DOCK8) in the autosomal-recessive form of hyper-IgE syndrome. J Allergy Clin Immunol, 124(6), 1289-1302.e1284. doi:10.1016/j.jaci.2009.10.038

Ferenczy, M. W., Marshall,
L. J., Nelson, C. D., Atwood, W. J., Nath, A., Khalili, K., & Major, E. O. (2012). Molecular biology, epidemiology, and pathogenesis of progressive multifocal leukoencephalopathy, the JC virus-induced demyelinating disease of the human brain. Clin Microbiol Rev, 25(3), 471-506. doi:10.1128/cmr.05031-11

Freeman, A. F.,
Gonzalez, C. E., Yates, B., Cole, K., Little, L., Flannelly, E., . . . Shah, N. N. (2025). Hematopoietic cell transplantation for DOCK8 deficiency: Results from a prospective clinical trial. J Allergy Clin Immunol, 155(1), 176-187. doi:10.1016/j.jaci.2024.08.021

Ganesan, K., Duraisamy,
S., Nair, A., Muthukumar, V., Swaminathan, V. V., Jayakumar, I., . . . Raj, R. (2024). Emerging Spectrum of DOCK8 Deficiency in Children and Challenges Associated with Providing Treatment. Indian J Pediatr, 91(8), 861. doi:10.1007/s12098-024-05070-9

Griggs, B. L., Ladd, S., Saul,
R. A., DuPont, B. R., & Srivastava, A. K. (2008). Dedicator of cytokinesis 8 is disrupted in two patients with mental retarda-

tion and developmental disabilities. Genomics, 91(2), 195-202. doi:10.1016/j.ygeno.2007.10.011

Hadjadj, J., Guffroy, A., Delavaud,
C., Taieb, G., Meyts, I., Fresard, A., . . . Suarez, F. (2019). Progressive Multifocal Leukoencephalopathy in Primary Immunodeficiencies. J Clin Immunol, 39(1), 55-64. doi:10.1007/s10875-018-0578-8

Ibrahim, H., Maksod, S. A., Khorshed,
M., Rady, H., Haron, M., Alkassas, O., . . . Mohamed, A. (2023). Association of hyper IgE with herpetic viral encephalitis and ecthyma gangrenosum in a male Egyptian patient. The Egyptian Journal of Internal Medicine, 35(1), 2. doi:10.1186/s43162-022-00186-w

Khayat, A. M., Alshareef, B. G., Alharbi
S. F., AlZahrani, M. M., Alshangity, B. A., & Tashkandi, N. F. (2024). Consanguineous Marriage and Its Association With Genetic Disorders in Saudi Arabia: A Review. Cureus, 16(2), e53888. doi:10.7759/cureus.53888

Kose, H., Karali, Z., Bodur, M.,
Cekic, S., & Kilic, S. S. (2024). Neurological involvement in patients with primary immunodeficiency. Allergologia et Immunopathologia, 52(1), 85-92.

Krgovic, D., Kokalj Vokac, N.,
Zagorac, A., & Gregoric Kumperscak, H. (2018). Rare structural variants in the DOCK8 gene identified in a cohort of 439 patients with neurodevelopmental disorders. Scientific Reports, 8(1), 9449.

Kumar Jindal, A., Sil, A., Aggarwal,
R., Tyagi, R., Mondal, S., Singh, A., . . . Singh, S. (2024). Clinical, immunological and molecular profiles of DOCK8 deficiency in six patients from a tertiary care centre in North India. Clinical and Experimental Dermatology, 49(3), 226-234. doi:10.1093/ced/llad345

Lambe, T., Crawford, G., Johnson,
A. L., Crockford, T. L., Bouriez-Jones, T., Smyth, A. M., . . . Cornall, R. J. (2011). DOCK8 is essential for T-cell survival and the maintenance of CD8+ T-cell memory. Eur J Immunol, 41(12), 3423-3435. doi:10.1002/eji.201141759

Liquidano-Perez, E., Maza-Ramos,
G., Perez Arias, B. A., Lugo Reyes, S. O., Barragan Arevalo, T., Solorzano-Morales, S. A., . . . Gonzalez-Serrano, M. E. (2024). Clinical, immunological, and genetic description of a Mexican cohort of patients with DOCK8 deficiency. Pediatr Allergy Immunol, 35(2), e14073. doi:10.1111/pai.14073

Liquidano-Pérez, E., Maza-Ramos,
G., Yamazaki-Nakashimada, M. A., Barragán-Arévalo, T., Lugo-Reyes, S. O., Scheffler-Mendoza, S., . . . González-Serrano, M. E. (2022). [Combined immunodeficiency due to DOCK8 deficiency. State of the art]. Rev Alerg Mex, 69(1), 31-47. doi:10.29262/ram.v69i1.1104

Pillay, B. A., Avery, D. T., Smart,
J. M., Cole, T., Choo, S., Chan, D., . . . Phan, T. G. (2019). Hematopoietic stem cell transplant effectively rescues lymphocyte differentiation and function in DOCK8-deficient patients. JCI insight, 4(11).

Randall, K. L., Lambe,
T., Goodnow, C. C., & Cornall, R. J. (2010). The essential role of DOCK8 in humoral immunity. Disease markers, 29(3-4), 141-150.

Ruusala, A., & Aspenström, P. (2004).
Isolation and characterisation of DOCK8, a member of the DOCK180-related regulators of cell morphology. FEBS Lett, 572(1-3), 159-166. doi:10.1016/j.febslet.2004.06.095

Singh, N., Ranganath, P., Jayaram,
A., Jhawar, P., Kotecha, U., Janardhanan, J., . . . Bhattad, S. (2024). Clinical and molecular profile of 20 patients with DOCK8 deficiency-a single-center experience from Southern India. Immunol Res, 73(1), 8. doi:10.1007/s12026-024-09571-9

Tangye, S. G., Pillay, B., Randall,
K. L., Avery, D. T., Phan, T. G., Gray, P., . . . Arkwright, P. D. (2017). Dedicator of cytokinesis 8–deficient CD4+ T cells are biased to a TH2 effector fate at the expense of TH1 and TH17 cells. Journal of Allergy and Clinical Immunology, 139(3), 933-949.

Yang, J., & Liu, Y. (2021).
Autosomal recessive hyper-IgE syndrome caused by DOCK8 gene mutation with new clinical features: a case report. BMC Neurol, 21(1), 288. doi:10.1186/s12883-021-02324-3

Yang, J., & Liu, Y. (2021).
Autosomal recessive hyper-IgE syndrome caused by DOCK8 gene mutation with new clinical features: a case report. BMC Neurology, 21(1), 288. doi:10.1186/s12883-021-02324-3

Yildirim, M., Ayvaz, D. C., Konuskan,
B., Gocmen, R., Tezcan, I., Topcu, M., . . . Anlar, B. (2018). Neurologic involvement in primary immunodeficiency disorders. Journal of Child Neurology, 33(5), 320-328.

Zhang, L., Cao, Y., Dai, X., & Zhang, X. (2022).
Deciphering the role of DOCK8 in tumorigenesis by regulating immunity and the application of nanotechnology in DOCK8 deficiency therapy. Front Pharmacol, 13, 1065029. doi:10.3389/fphar.2022.1065029

Zhang, M., Cron, R. R., Chu, N., Nguyen,
J., Gordon, S. M., Eloseily, E. M., . . . Cron, R. Q. (2024). Role of DOCK8 in cytokine storm syndromes. Journal of Allergy and Clinical Immunology. doi
:https://doi.org/10.1016/j.jaci.2024.10.004

Zhang, Q., Davis, J. C., Lamborn,
I. T., Freeman, A. F., Jing, H., Favreau, A. J., . . . Su, H. C. (2009). Combined immunodeficiency associated with DOCK8 mutations. N Engl J Med, 361(21), 2046-2055. doi:10.1056/NEJMoa0905506

Zhang, Q., Jing, H., & Su, H. C. (2016).
Recent Advances in DOCK8 Immunodeficiency Syndrome. J Clin Immunol, 36(5), 441-449. doi:10.1007/s10875-016-0296-z