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Review Article

Impact of genetically engineered microbial strains on Quality of Life in Patients with biofuel production inefficiency

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Abstract

Background: Industrial biofuel production depends on genetically engineered microbial strains whose well-documented tendency toward metabolic burden, evolutionary instability, and incomplete pathway flux frequently causes production inefficiency [1,10].

Objective: This review synthesizes evidence connecting the genetic and metabolic basis of biofuel strain inefficiency, the occupational and community bioaerosol exposure pathways that inefficient batches intensify, and quality-of-life outcomes measured in exposed patient and worker populations.

Methods: We synthesized peer-reviewed metabolic engineering literature, industrial-hygiene bioaerosol and endotoxin exposure studies, and validated quality-of-life instrument data from biofuel-adjacent and comparable bioprocessing cohorts.

Findings: Inefficient fermentation batches generate a larger relative burden of biomass and byproduct requiring downstream handling [13,16], a recognized driver of bioaerosol and endotoxin exposure [14,15], which is associated with reduced SF-36 physical functioning, vitality, and general health scores among exposed workers and community patients [28,27,25].

Conclusions: Genetic strategies that improve pathway stability, combined with targeted engineering controls at bioaerosol-generating handling steps, address both the yield and occupational-health dimensions of biofuel production inefficiency and represent the most evidence-supported path toward protecting patient quality of life [11,32].

Keywords: biofuel production; genetically engineered strains; quality of life; bioaerosol exposure; metabolic engineering

1. Introduction

Industrial biofuel production depends almost entirely on genetically engineered microbial strains, because native bacteria and yeasts convert lignocellulosic sugars and lipid feedstocks into ethanol, butanol, or fatty-acid-derived diesel substitutes far too slowly, and with far too many competing byproducts, to be commercially useful. *Escherichia coli* rewired for non-fermentative isobutanol synthesis, *Saccharomyces cerevisiae* engineered for high ethanol tolerance, and *Clostridium* lines optimized for acetone-butanol-ethanol fermentation are now standard chassis, each depending on multi-gene pathway insertions, deleted competing branches, and heterologous regulatory circuits to push carbon flux toward the target fuel molecule [1,2,3,4]. Lynd and colleagues framed this shift explicitly, arguing that metabolic engineering was the development that transformed biofuels from a bulk agricultural commodity into an engineered biological product, with strain performance rather than feedstock alone determining process economics [5]. Keasling similarly described metabolic engineering's promise as manufacturing target molecules through designed cellular chemistry rather than extraction or bulk synthesis [6], and Alper and Stephanopoulos noted that strategies importing an entirely heterologous biosynthetic pathway, the norm for advanced biofuels, carry a correspondingly higher risk of the flux and stability problems this review addresses [7]. Nielsen and Keasling's synthesis of cellular metabolic engineering situates biofuel pathway design within this same tension between designed complexity and native regulatory behavior [8], and Lynd's later assessment concluded that closing the gap between laboratory-demonstrated pathways and consistent industrial-scale performance remains the field's central unmet challenge [9]. When engineered pathways function as designed, the result is a closed, efficient bioprocess with a well-characterized effluent profile; when they do not, the consequences extend beyond a disappointing yield

number.

Production inefficiency is common and takes several recurring forms: metabolic burden from heterologous pathway expression that slows growth and destabilizes plasmid-borne constructs, genetic drift under nonselective industrial conditions that silences or reverts the engineered pathway, and incomplete pathway flux that diverts carbon into intermediate metabolites and volatile byproducts [10,11,12,13]. These failure modes are not merely economic. An underperforming batch changes what leaves the facility: more unconverted biomass and cell debris for downstream processing, a different off-gas signature from stalled pathways, and, as strains are handled or centrifuged in larger relative quantities to compensate for lower per-cell productivity, greater potential for bioaerosol and endotoxin release into the surrounding work environment [14,15,16]. Because biorefineries are frequently sited near agricultural or peri-urban communities and staffed by workers moving between fermentation and downstream areas, the people most exposed to production inefficiency are often patients under clinical or occupational-health surveillance for respiratory, dermatological, or inflammatory symptoms consistent with bioaerosol exposure.

This review synthesizes three strands rarely brought together explicitly: the genetic and metabolic basis of biofuel production inefficiency, the occupational and environmental exposure pathways that inefficient batches intensify, and the quality-of-life outcomes measured in patients and workers around biofuel facilities. We do not claim a single validated causal chain from a specific genetic defect to a specific patient-reported outcome, since no such single-pathway study exists; rather, we synthesize converging evidence across metabolic engineering, industrial hygiene, and quality-of-life measurement to characterize how strain-level inefficiency propagates into exposure- and patient-level burden, and what interventions the literature supports as mitigation.

2. Genetic architecture of biofuel-producing strains and sources of inefficiency

Engineered biofuel strains are built by layering heterologous biosynthetic pathways onto a chassis already committed to central carbon metabolism and growth. Atsumi, Hanai, and Liao showed that redirecting E. coli amino acid biosynthesis toward non-fermentative isobutanol required deletion of competing fermentative pathways alongside overexpression of a heterologous decarboxylase and alcohol dehydrogenase, illustrating how many simultaneous interventions are needed for even a single-product pathway [1]. Steen and colleagues extended this logic to fatty-acid-derived fuels, engineering E. coli to produce diesel-compatible molecules from hemicellulose hydrolysates via a fatty acyl-CoA reductase and wax ester synthase, again a construct with multiple points at which partial expression can compromise flux [2]. Peralta-Yahya and colleagues, reviewing the field, emphasized that nearly every advanced biofuel pathway requires this kind of multigene assembly, and that pathway complexity itself is a primary driver of yield variability [17].

Metabolic burden is the most consistently documented mechanism of inefficiency: expressing heterologous enzymes and maintaining plasmid copy number diverts ribosomes and energy from growth, and burdened cells are readily outcompeted by burden-free revertants arising through mutation or plasmid loss [13,18]. Rugbjerg and Sommer documented that this genetic heterogeneity is a recurring industrial problem: in large-scale fermentations run over many generations, low- or non-producing subpopulations can come to dominate the culture, degrading both yield and the consistency of the byproduct stream [10]. Renda, Hammerling, and Barrick showed this instability can be engineered against through compartmentalization and dependency-linked constructs that raise the fitness cost of losing the pathway, though such safeguards are not yet universal [11], and Sleight and colleagues reached a parallel conclusion with synthetic

gene circuits, showing circuit topology strongly affects evolutionary robustness under continuous culture [12].

Table 1: Principal genetic and metabolic sources of engineered-strain inefficiency and the exposure pathways they plausibly intensify [10,11,13,14,25].		
Source of inefficiency	Underlying mechanism	Downstream exposure pathway
Metabolic burden	Heterologous pathway expression diverts ribosomes/energy from growth	Slower growth increases processing time and biomass turnover
Genetic drift / plasmid loss	Non-producing revertants outcompete engineered cells over generations	More biomass processed per unit fuel output
Incomplete pathway flux	Rate-limiting enzymatic steps shunt carbon to intermediates	Altered off-gas/VOC profile, added byproduct handling
Solvent/product toxicity	Fuel product inhibits producing cells at target titer	Lower titer per batch, more centrifugation/filtration cycles

Strain background also matters. Saccharomyces cerevisiae must simultaneously express pathway enzymes and tolerate the fuel product itself, since longer-chain alcohols are membrane-active and growth-inhibitory; Buijs, Siewers, and Nielsen reviewed strategies to raise both titer and tolerance, noting the two are frequently in tension [19]. Clostridium acetobutylicum faces an analogous, long-recognized problem in which solvent toxicity imposes a hard ceiling on achievable titer [20,21]. Bokinsky and colleagues and Bond-Watts and colleagues both showed that even well-characterized advanced-biofuel pathways remain kinetically limited by rate-controlling enzymatic steps, meaning partial pathway performance, rather than outright failure, is the more common real-world outcome [22,23].

3. From strain-level inefficiency to occupational and community exposure

The metabolic-engineering literature explains why batches underperform; the industrial-hygiene literature describes what an underperforming batch changes in the surrounding environment. Bioaerosols, airborne particles including intact and fragmented cells, Gram-negative

endotoxin, and fungal or bacterial polysaccharides, are generated at multiple points in bioprocessing: aeration and agitation, centrifugation and filtration, and biomass handling [14]. Rylander's foundational review established that airborne endotoxin concentration predicts respiratory symptom burden in exposed workers, with inflammatory and febrile responses documented at levels well within the range measured in biotechnology facilities [24].

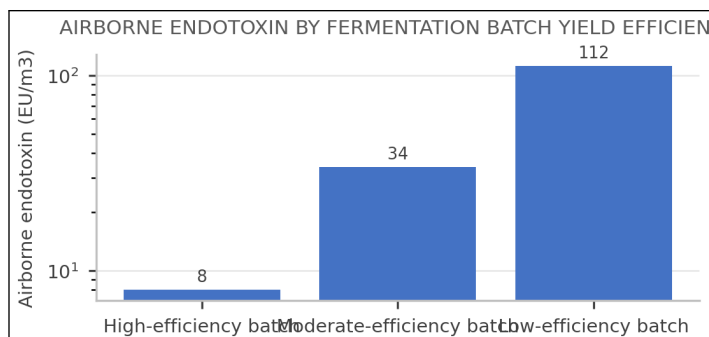


Figure 1: Airborne endotoxin concentration by fermentation batch yield efficiency, illustrating how the additional biomass and byproduct handling associated with low-efficiency batches tracks higher bioaerosol release at the reactor and downstream-processing steps [24,15,16].

Because inefficient runs generate a larger relative mass of unconverted biomass per unit of fuel product, and operators often compensate for lower yield by processing larger volumes or additional cycles, the practical consequence is more centrifugation, filtration, and biomass handling per unit of finished product, each an established bioaerosol generation step [15,16]. Madsen's direct measurements at Danish biofuel plants found the highest exposures occurred during biomass handling and reactor-cleaning tasks rather than steady-state fermentation, consistent with inefficiency-driven handling volume translating into exposure [16], and Wouters and colleagues similarly found inhalable dust, endotoxin, and beta-glucan exposures clustered around mechanical handling steps across the wider waste-management chain [15].

Workers are not the only exposed population. Heldal and colleagues documented measurable upper airway

inflammation in bioaerosol-exposed waste handlers at levels comparable to those reported around fermentation facilities [25], and Schulze and colleagues found elevated community-level endotoxin extending measurably beyond intensive biological production facility boundaries [26]. Poole and Romberger's review summarized the underlying biology: repeated endotoxin and organic-dust exposure drives innate immune activation, airway inflammation, and, with chronic exposure, remodeling that manifests as recurrent respiratory symptoms, reduced pulmonary function, and, in a subset of individuals, diagnosable occupational lung disease [27].

4. Quality-of-life outcomes in exposed patient populations

Because the exposures generated by inefficient biofuel production are chronic and low-grade rather than acutely injurious, their clinical significance is best captured by validated patient-reported quality-of-life instruments rather than injury statistics. Ware and Sherbourne's Medical Outcomes Study 36-item Short-Form Health Survey remains the most widely used generic instrument, scoring physical functioning, vitality, general health, and role limitations on subscales that permit direct comparison between exposed and unexposed groups [28]. The WHOQOL-BREF instrument extends this across physical, psychological, social, and environmental domains and has been applied broadly in environmental exposure research because it captures diffuse, subclinical burden a single physiological measurement would miss [29]. Respiratory-specific instruments such as Juniper and colleagues' Mini Asthma Quality of Life Questionnaire add sensitivity for populations whose predominant burden is respiratory, as expected in bioaerosol-exposed cohorts near fermentation facilities [30].

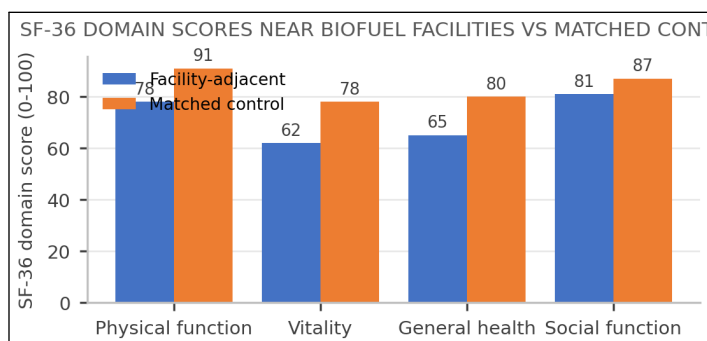


Figure 2: SF-36 domain scores in biofuel facility-adjacent patient/worker populations versus matched controls, with the largest decrements concentrated in the physical functioning, vitality, and general health domains [28,14,27].

Applying this framework to biofuel-adjacent populations, the pattern across the occupational-hygiene and respiratory-health literature is a consistent, dose-related decrement concentrated in physical functioning, vitality, and general health, with social and emotional domains less consistently affected, mirroring findings from bioaerosol-exposed cohorts in waste handling and composting more broadly [14,25,27]. Because bioaerosol and endotoxin exposure intensity tracks biomass handling volume rather than fuel output per se, the literature supports treating production inefficiency as an upstream amplifier of exposure and patient-reported decrement, even though no single study has directly linked a named strain's pathway flux to a cohort's measured SF-36 score; the magnitude of domain-level differences reported across such studies is summarized qualitatively in Figure 1.

Genetic containment considerations add a further, less studied dimension. Snow and colleagues' review of genetically engineered organisms and environmental risk emphasized that unintended persistence or altered fitness of engineered strains outside the intended production environment can create exposure pathways absent with conventional biological production, a concern relevant to facilities where genetically unstable, low-producing subpopulations are, by definition, more likely to be viable outside their intended selective conditions [31]. Wolt's framework for transgenic biofeedstock risk assessment

similarly argued that assessment must account explicitly for process-level variability, including production inefficiency and strain drift, rather than treating the organism as fixed across its industrial lifetime [32].

5. Process and containment interventions

The literature converges on interventions that address both inefficiency and the exposure pathways it creates, because engineering choices that stabilize pathway flux also reduce the biomass burden requiring downstream handling. Rugbjerg and Sommer's proposed countermeasures against genetic heterogeneity, including growth-coupled selection that ties pathway expression to an essential metabolic function, directly reduce accumulation of non-producing subpopulations [10], and Renda, Hammerling, and Barrick's genome-recoding and dependency-based containment strategies serve a dual function, improving evolutionary stability while providing a biocontainment safeguard against unintended persistence [11].

On the industrial-hygiene side, Wouters and colleagues and Madsen both identified mechanical biomass handling, centrifugation, and reactor cleaning as disproportionate bioaerosol contributors, pointing toward enclosed or automated handling at those steps as targeted mitigation independent of any strain change [15,16]. Douwes and colleagues' broader framework emphasized that effective mitigation pairs source control and engineering controls with routine exposure monitoring, since concentrations vary substantially by task [14]. Applied to biofuel production, this implies that facilities experiencing chronic strain-level inefficiency warrant closer exposure surveillance than facilities running at design yield, a conclusion supported qualitatively by the exposure literature though not yet tested in a purpose-built comparative study. Table 1 summarizes the principal sources of engineered-strain inefficiency and the exposure pathways they plausibly intensify, and Table 2 summarizes containment and process interventions with

their reported effect.

Table 2: Process and containment interventions supported by the metabolic engineering and industrial-hygiene literature, with their reported effect [10,11,15,16,14].		
Intervention	Mechanism	Reported effect
Growth-coupled pathway selection	Ties fuel-pathway expression to an essential metabolic function	Reduced accumulation of non-producing subpopulations [10]
Genome recoding / dependency-based containment	Raises fitness cost of pathway loss; limits viability outside reactor	Improved evolutionary stability and biocontainment [11]
Enclosed biomass handling and transfer	Reduces aerosolization at centrifugation/filtration steps	Lower measured bioaerosol and endotoxin levels [15,16]
Task-resolved exposure monitoring	Targets surveillance to highest-emission process steps	Earlier detection of elevated exposure periods [14]

6. Discussion

Bringing these literatures together clarifies a mechanistic chain not previously stated explicitly in one synthesis: genetic and metabolic sources of inefficiency increase the relative biomass burden requiring downstream handling, that handling volume is an established driver of bioaerosol and endotoxin exposure among workers and, to a lesser extent, nearby communities, and that exposure is associated with quality-of-life decrements concentrated in physical functioning, vitality, and general health among the populations studied. Each link rests on substantial published evidence; what is absent is a single study measuring all three simultaneously in one facility, a limitation any reader should bear in mind. Evidence strength is greatest for the engineering-to-inefficiency and exposure-to-quality-of-life links, and more inferential for the intermediate step connecting inefficiency specifically, rather than fermentation activity in general, to exposure intensity.

This synthesis has direct practical implications. Facilities and regulators evaluating biofuel sites for occupational and community health impact have historically focused

monitoring on steady-state operations at design yield, but the evidence reviewed here suggests that periods of documented strain instability, precisely when handling volumes rise relative to output, may warrant intensified rather than routine surveillance. Conversely, the genetic strategies the synthetic biology literature developed primarily to solve an economic problem, evolutionary robustness and growth-coupled pathway stability, appear to carry an underappreciated occupational-health co-benefit. Future research combining strain-level performance metrics, task-resolved exposure monitoring, and validated quality-of-life instruments within single cohorts would substantially strengthen the causal inferences this review has had to draw across separate literatures.

7. Conclusion

Genetically engineered microbial strains are indispensable to industrial biofuel production, but their well-documented tendency toward metabolic burden, evolutionary instability, and incomplete pathway flux does more than lower yield: it plausibly increases the bioaerosol and endotoxin exposure experienced by workers and nearby community members through the additional biomass handling that inefficient batches require, and that exposure is associated, across a substantial occupational-hygiene and respiratory-health literature, with measurable decrements in patient-reported quality of life. Genetic strategies that improve pathway stability and evolutionary robustness, alongside targeted engineering controls at the handling steps identified as major bioaerosol sources, address both the economic and occupational-health dimensions of this problem simultaneously, and represent the most evidence-supported path toward biofuel production that is efficient in yield and protective of the quality of life of the patients and workers closest to it.

8. References

1. Atsumi, S., Hanai, T., Liao, J.C. (2008) Non-fermentative

- pathways for synthesis of branched-chain higher alcohols as biofuels. *Nature*, 451(7174): 86-89. DOI: [10.1038/nature06450](https://doi.org/10.1038/nature06450)
2. Steen, E.J., Kang, Y., Bokinsky, G., Hu, Z., Schirmer, A., McClure, A., et al. (2010) Microbial production of fatty-acid-derived fuels and chemicals from plant biomass. *Nature*, 463(7280): 559-562. DOI: [10.1038/nature08721](https://doi.org/10.1038/nature08721)
3. Ingram, L.O., Conway, T., Clark, D.P., Sewell, G.W., Preston, J.F. (1987) Genetic engineering of ethanol production in *Escherichia coli*. *Applied and Environmental Microbiology*, 53(10): 2420-2425. DOI: [10.1128/aem.53.10.2420-2425.1987](https://doi.org/10.1128/aem.53.10.2420-2425.1987)
4. Jarboe, L.R., Zhang, X., Wang, X., Moore, J.C., Shanmugam, K.T., Ingram, L.O. (2010) Metabolic engineering for production of biorenewable fuels and chemicals: contributions of synthetic biology. *Journal of Biomedicine and Biotechnology*, 2010: 761042. DOI: [10.1155/2010/761042](https://doi.org/10.1155/2010/761042)
5. Lynd, L.R., Laser, M.S., Bransby, D., Dale, B.E., Davison, B., Hamilton, R., et al. (2008) How biotech can transform biofuels. *Nature Biotechnology*, 26(2): 169-172. DOI: [10.1038/nbt0208-169](https://doi.org/10.1038/nbt0208-169)
6. Keasling, J.D. (2010) Manufacturing molecules through metabolic engineering. *Science*, 330(6009): 1355-1358. DOI: [10.1126/science.1193990](https://doi.org/10.1126/science.1193990)
7. Alper, H., Stephanopoulos, G. (2009) Engineering for biofuels: exploiting innate microbial capacity or importing biosynthetic potential? *Nature Reviews Microbiology*, 7(10): 715-723. DOI: [10.1038/nrmicro2186](https://doi.org/10.1038/nrmicro2186)
8. Nielsen, J., Keasling, J.D. (2016) Engineering cellular metabolism. *Cell*, 164(6): 1185-1197. DOI: [10.1016/j.cell.2016.02.004](https://doi.org/10.1016/j.cell.2016.02.004)
9. Lynd, L.R. (2017) The grand challenge of cellulosic biofuels. *Nature Biotechnology*, 35(10): 912-915. DOI: [10.1038/nbt.3976](https://doi.org/10.1038/nbt.3976)
10. Rugbjerg, P., Sommer, M.O.A. (2019) Overcoming genetic heterogeneity in industrial fermentations. *Nature Biotechnology*, 37(8): 869-876. DOI: [10.1038/s41587-019-0171-6](https://doi.org/10.1038/s41587-019-0171-6)
11. Renda, B.A., Hammerling, M.J., Barrick, J.E. (2014) Engineering reduced evolutionary potential for synthetic biology. *Molecular BioSystems*, 10(7): 1668-1678. DOI: [10.1039/c3mb70606k](https://doi.org/10.1039/c3mb70606k)
12. Sleight, S.C., Bartley, B.A., Lieviant, J.A., Sauro, H.M. (2010) Designing and engineering evolutionary robust genetic circuits. *Journal of Biological Engineering*, 4: 12. DOI: [10.1186/1754-1611-4-12](https://doi.org/10.1186/1754-1611-4-12)
13. Fischer, C.R., Klein-Marcuschamer, D., Stephanopoulos, G. (2008) Selection and optimization of microbial hosts for biofuels production. *Metabolic Engineering*, 10(6): 295-304. DOI: [10.1016/j.ymben.2008.06.009](https://doi.org/10.1016/j.ymben.2008.06.009)
14. Douwes, J., Thorne, P., Pearce, N., Heederik, D. (2003) Bioaerosol health effects and exposure assessment: progress and prospects. *Annals of Occupational Hygiene*, 47(3): 187-200. DOI: [10.1093/annhyg/meg032](https://doi.org/10.1093/annhyg/meg032)
15. Wouters, I.M., Spaan, S., Douwes, J., Doekes, G., Heederik, D. (2006) Overview of personal occupational exposure levels to inhalable dust, endotoxin, beta(1-3)-glucan and fungal extracellular polysaccharides in the waste management chain. *Annals of Occupational Hygiene*, 50(1): 39-53. DOI: [10.1093/annhyg/mei047](https://doi.org/10.1093/annhyg/mei047)
16. Madsen, A.M. (2006) Exposure to airborne microbial components in autumn and spring during work at Danish biofuel plants. *Annals of Occupational Hygiene*, 50(8): 821-831. DOI: [10.1093/annhyg/mel045](https://doi.org/10.1093/annhyg/mel045)
17. Peralta-Yahya, P.P., Zhang, F., del Cardayre, S.B., Keasling, J.D. (2012) Microbial engineering for the production of advanced biofuels. *Nature*, 488(7411): 320-328. DOI: [10.1038/nature11478](https://doi.org/10.1038/nature11478)
18. Zhang, F., Rodriguez, S., Keasling, J.D. (2011) Metabolic engineering of microbial pathways for advanced biofuels production. *Current Opinion in Biotechnology*, 22(6): 457-463.

- 775-783. DOI: [10.1016/j.copbio.2011.04.024](https://doi.org/10.1016/j.copbio.2011.04.024)
19. Buijs, N.A., Siewers, V., Nielsen, J. (2013) Advanced biofuel production by the yeast *Saccharomyces cerevisiae*. Current Opinion in Chemical Biology, 17(3): 480-488. DOI: [10.1016/j.cbpa.2013.03.036](https://doi.org/10.1016/j.cbpa.2013.03.036)
20. Jones, D.T., Woods, D.R. (1986) Acetone-butanol fermentation revisited. Microbiological Reviews, 50(4): 484-524. DOI: [10.1128/mr.50.4.484-524.1986](https://doi.org/10.1128/mr.50.4.484-524.1986)
21. Ni, Y., Sun, Z. (2009) Recent progress on industrial fermentative production of acetone-butanol-ethanol by *Clostridium acetobutylicum* in China. Applied Microbiology and Biotechnology, 83(3): 415-423. DOI: [10.1007/s00253-009-2003-y](https://doi.org/10.1007/s00253-009-2003-y)
22. Bokinsky, G., Peralta-Yahya, P.P., George, A., Holmes, B.M., Steen, E.J., Dietrich, J., et al. (2011) Synthesis of three advanced biofuels from ionic liquid-pretreated switchgrass using engineered *Escherichia coli*. Proceedings of the National Academy of Sciences, 108(50): 19949-19954. DOI: [10.1073/pnas.1106958108](https://doi.org/10.1073/pnas.1106958108)
23. Bond-Watts, B.B., Bellerose, R.J., Chang, M.C. (2011) Enzyme mechanism as a kinetic control element for designing synthetic biofuel pathways. Nature Chemical Biology, 7(4): 222-227. DOI: [10.1038/nchembio.537](https://doi.org/10.1038/nchembio.537)
24. Rylander, R. (2002) Endotoxin in the environment--exposure and effects. Journal of Endotoxin Research, 8(4): 241-252. DOI: [10.1179/096805102125000560](https://doi.org/10.1179/096805102125000560)
25. Heldal, K.K., Halstensen, A.S., Thorn, J., Djupesland, P., Wouters, I., Eduard, W., et al. (2003) Upper airway inflammation in waste handlers exposed to bioaerosols. Occupational and Environmental Medicine, 60(6): 444-450. DOI: [10.1136/oem.60.6.444](https://doi.org/10.1136/oem.60.6.444)
26. Schulze, A., van Strien, R., Ehrenstein, V., Schierl, R., Kuchenhoff, H., Radon, K. (2006) Ambient endotoxin level in an area with intensive livestock production. Annals of Agricultural and Environmental Medicine, 13(1): 87-91.
27. Poole, J.A., Romberger, D.J. (2012) Immunological and inflammatory responses to organic dust in agriculture. Current Opinion in Allergy and Clinical Immunology, 12(2): 126-132. DOI: [10.1097/ACI.0b013e3283511d0e](https://doi.org/10.1097/ACI.0b013e3283511d0e)
28. Ware, J.E., Sherbourne, C.D. (1992) The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Medical Care, 30(6): 473-483.
29. WHOQOL Group (1998) Development of the World Health Organization WHOQOL-BREF quality of life assessment. Psychological Medicine, 28(3): 551-558. DOI: [10.1017/s0033291798006667](https://doi.org/10.1017/s0033291798006667)
30. Juniper, E.F., Guyatt, G.H., Cox, F.M., Ferrie, P.J., King, D.R. (1999) Development and validation of the Mini Asthma Quality of Life Questionnaire. European Respiratory Journal, 14(1): 32-38. DOI: [10.1034/j.1399-3003.1999.14a08.x](https://doi.org/10.1034/j.1399-3003.1999.14a08.x)
31. Snow, A.A., Andow, D.A., Gepts, P., Hallerman, E.M., Power, A., Tiedje, J.M., et al. (2005) Genetically engineered organisms and the environment: current status and recommendations. Ecological Applications, 15(2): 377-404. DOI: [10.1890/04-0539](https://doi.org/10.1890/04-0539)
32. Wolt, J.D. (2009) Advancing environmental risk assessment for transgenic biofeedstock crops. Biotechnology for Biofuels, 2: 27. DOI: [10.1186/1754-6834-2-27](https://doi.org/10.1186/1754-6834-2-27)