

in rural hospitals. Thus we are confident that our proposals can be implemented in the more advanced centres in the places that have been specifically set up for the treatment of MDR-TB. There can be nothing special about achieving the same individualisation in the treatment for MDR-TB, as long as clinicians in those places are trained for the Bayesian-dose optimisation process. Indeed, we consider this approach less costly than losing patients to MDR and XDR-TB, and the cost of secondary cases.



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Bayesian-dose optimisation for better and cost effective treatment of multi- and extremely drug resistant tuberculosis <http://ow.ly/pN6KC>

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References

- 1 Migliori GB, Sotgiu G, Gandhi NR, *et al.* Drug resistance beyond extensively drug-resistant tuberculosis: individual patient data meta-analysis. *Eur Respir J* 2013; 42: 169–179.
- 2 Srivastava S, Peloquin CASG, Migliori GB. Therapeutic drug management: is it the future of MDR-TB treatment? *Eur Respir J* 2013; 42: 1449–1453.
- 3 Akkerman AO, Van Altena R, Klinkenberg T, *et al.* Drug concentration in lung tissue in multidrug resistant tuberculosis. *Eur Respir J* 2013; 42: 1750–1752.
- 4 Gumbo T. New susceptibility breakpoints for first-line antituberculosis drugs based on antimicrobial pharmacokinetic/pharmacodynamic science and population pharmacokinetic variability. *Antimicrob Agents Chemother* 2010; 54: 1484–1491.
- 5 Gumbo T, Siyambalapitiyage Dona CSW, Leef R. Pharmacokinetics-pharmacodynamics of pyrazinamide in a novel *in vitro* model of tuberculosis for sterilizing effect: a paradigm for faster assessment of new antituberculosis drugs. *Antimicrob Agents Chemother* 2009; 53: 3197–3204.
- 6 Gumbo T, Louie A, Deziel MR, *et al.* Selection of a moxifloxacin dose that suppresses drug resistance in *Mycobacterium tuberculosis*, by use of an *in vitro* pharmacodynamic infection model and mathematical modeling. *J Infect Dis* 2004; 190: 1642–1651.
- 7 Srivastava S, Pasipanodya JG, Meek C, *et al.* Multidrug-resistant tuberculosis not due to noncompliance but to between-patient pharmacokinetic variability. *J Infect Dis* 2011; 204: 1951–1959.
- 8 Bolhuis MS, Altena R, van Soolingen D, *et al.* Clarithromycin increases linezolid exposure in multidrug-resistant tuberculosis patients. *Eur Respir J* 2013; 42: 000–000.
- 9 Sotgiu G, Centis R, D'Ambrosio L, *et al.* Efficacy, safety and tolerability of linezolid containing regimens in treating MDR-TB and XDR-TB: systematic review and meta-analysis. *Eur Respir J* 2012; 40: 1430–1442.
- 10 Haverkamp W, Kruesmann F, Fritsch A, *et al.* Update on the cardiac safety of moxifloxacin. *Curr Drug Saf* 2012; 7: 149–163.

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MicroRNAs and pulmonary hypertension

To the Editor:

MicroRNAs have emerged as important posttranscriptional regulators of gene transcription. The interesting review by RUPANI *et al.* [1] on microRNAs in respiratory diseases is, thus, accurately timed. We use this opportunity to additionally mention the role of microRNAs in pulmonary hypertension, which has been investigated both in experimental models and in human disease and, as recently reviewed in the *European Respiratory Journal* [2], might be of pathogenetic relevance for pulmonary hypertension. Caruso *et al.* [3], for example, described alterations in the expression of dicer, which is one of the most important microRNA processing enzymes, probably explaining the reduced expression levels of several microRNAs in patients with pulmonary hypertension. Some of these, such as miR-150 [4], have been described as independent predictors for an adverse outcome. Others, including miR-204 [5] have been linked to important signalling pathways in pulmonary arterial smooth muscle cells. Finally, our own work, has identified the microRNA cluster 17/92 as directly targeting the bone morphogenetic protein receptor type II [6], which, as shown by successful inhibition by antagomirs *in vivo* [7, 8], could be a causative therapeutic approach for the vascular remodelling of pulmonary arteries.



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The importance of microRNAs in respiratory diseases includes their pathogenetic role and the use as biomarkers in PH <http://ow.ly/o3S8c>

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References

- 1 Rupani H, Sanchez-Elsner T, Howarth P. MicroRNAs and respiratory diseases. *Eur Respir J* 2013; 41: 695–705.
- 2 Voelkel NF, Gomez-Arroyo J, Abbate A, *et al.* Pathobiology of pulmonary arterial hypertension and right ventricular failure. *Eur Respir J* 2012; 40: 1555–1565.
- 3 Caruso P, MacLean MR, Khanin R, *et al.* Dynamic changes in lung microRNA profiles during the development of pulmonary hypertension due to chronic hypoxia and monocrotaline. *Arterioscler Thromb Vasc Biol* 2010; 30: 716–723.
- 4 Rhodes CJ, Wharton J, Boon RA, *et al.* Reduced microRNA-150 is associated with poor survival in pulmonary arterial hypertension. *Am J Respir Crit Care Med* 2013; 187: 294–302.
- 5 Courboulin A, Paulin R, Giguère NJ, *et al.* Role for miR-204 in human pulmonary arterial hypertension. *J Exp Med* 2011; 208: 535–548.
- 6 Brock M, Trenkmann M, Gay RE, *et al.* Interleukin-6 modulates the expression of the bone morphogenic protein receptor type II through a novel STAT3-microRNA cluster 17/92 pathway. *Circ Res* 2009; 104: 1184–1191.
- 7 Pullamsetti SS, Doebele C, Fischer A, *et al.* Inhibition of microRNA-17 improves lung and heart function in experimental pulmonary hypertension. *Am J Respir Crit Care Med* 2012; 185: 409–419.
- 8 Brock M, Samillan VJ, Trenkmann M, *et al.* AntagomiR directed against miR-20a restores functional BMPR2 signalling and prevents vascular remodelling in hypoxia-induced pulmonary hypertension. *Eur Heart J* 2012 [In press DOI: 10.1093/eurheartj/ehs060].

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