

## Total adenosine deaminase highly correlated with adenosine deaminase 2 activity in serum

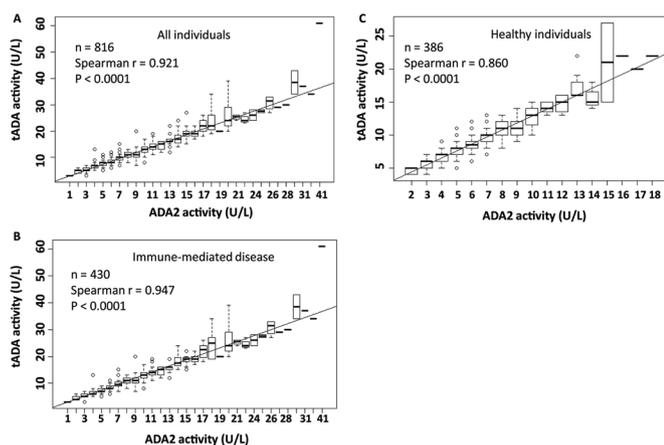
We read with great interest the article published by Lee and colleagues<sup>1</sup> presenting the potential diagnostic value of adenosine deaminase 2 (ADA2) in systemic juvenile idiopathic arthritis (sJIA) with macrophage activation syndrome (MAS). Their study examined ADA2 activity in children with inflammatory and immune-mediated diseases. By comparing normal ranges of ADA2 in healthy individuals, their finding identified the utility of plasma ADA2 activity as a biomarker of MAS. ADA2 activity were measured by a spectrophotometric assay in the presence of a selective inhibitor of ADA1, erythro-9-amino- $\beta$ -hexyl- $\alpha$ -methyl-9-ethanol hydrochloride (EHNA). We support the views expressed by the authors that ADA2 detection could be helpful in the diagnosis of MAS in sJIA. Here, we would like to share with the authors our data of ADA activity detection.

As we know, ADA contains two isoenzymes: ADA1 and ADA2. In plasma, ADA2 is a major component of total adenosine deaminase (tADA).<sup>2,3</sup> tADA activity detection has been carried out in the clinical laboratory for many years, which was usually used for differential diagnosis of benign and malignant effusions.<sup>4</sup> The measurement method of tADA activity is simpler than ADA2 activity. Here, we report the correlation between tADA and ADA2 activity in the serum of healthy individuals and patients with immune-mediated diseases. Serum tADA activity was measured with an enzymatic method kit (Sichuan Maccura Biotechnology, China), adapted to the automated biochemistry analyser (Hitachi 7600, Japan).<sup>5</sup> Serum ADA2 activity was measured in the presence of 0.1 mM EHNA. We determined serum tADA and ADA2 activity in 386 healthy individuals and 430 patients with different immune-mediated diseases, including rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis, myasthenia gravis and autoimmune liver diseases.

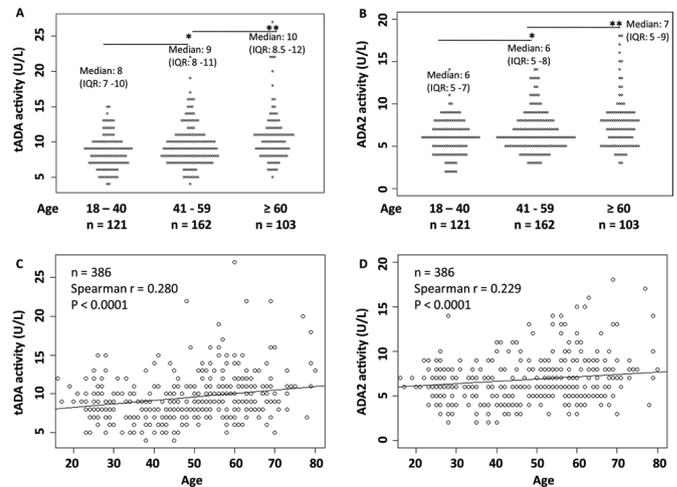
First, we found that tADA levels highly correlated with ADA2 in 816 individuals (figure 1A;  $r=0.921$ ,  $p<0.0001$ ). Notably, the correlation coefficient between tADA and ADA2 in patients with immune-mediated diseases (figure 1B;  $r=0.947$ ,  $p<0.0001$ ) was higher than that in healthy individuals (figure 1C;  $r=0.860$ ,  $p<0.0001$ ). Thus, like ADA2 activity, tADA activity might also be a biomarker of MAS. Due to convenient detection, tADA activity would be more suitable for clinical application than ADA2.

Second, in the study of Lee *et al.*,<sup>1</sup> they showed that ADA2 activity was higher in children than in adults (age 18 years and older), with an overall negative correlation with age ( $r=-0.250$ ,  $p<0.0001$ ). Here, we analysed the distribution of tADA and ADA2 activity in adults. The results showed that tADA and ADA2 activity were higher in elderly people (age  $\geq 60$  years) than young adults (figure 2A,B;  $p<0.01$ ), with an overall positive correlation with age (figure 2C,D;  $p<0.0001$ ). Because ADA plays an important role in the immune system, these combined data indicated the potential difference of the immune system status between children, elderly people and other adults.

In conclusion, the high correlation between tADA and ADA2 activity supports the clinical application value of tADA detection. Further studies are



**Figure 1** Correlation between serum ADA2 and tADA activity was calculated by Spearman's rank correlation analysis. (A–C) Correlation between ADA2 and tADA in all 816 individuals, 430 patients with immune-mediated diseases and 385 healthy individuals. ADA2, adenosine deaminase 2; tADA, total adenosine deaminase.



**Figure 2** Determination of serum tADA and ADA2 activity in healthy adults. (A,B) Plot comparing serum tADA and ADA2 activity in adults stratified by age. (C,D) Correlation between serum tADA, ADA2 activity and age. \* $p<0.05$ , \*\* $p<0.01$ . ADA2, adenosine deaminase 2; tADA, total adenosine deaminase.

needed to validate the effect and mechanism of higher level of ADA activity in children and elderly people.

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