

expressed genes (DEGs) in PBMC between severe and mild COVID-19 patients. The transcriptome of severe COVID-19 patients was compared with the data on the transcriptional changes observed in our six-month study. After filtering the DEGs for  $p$ -value  $<0.05$  and fold change  $>1.5$ , folate receptor 3 (*FOLR3*) was found to be a gene whose expression was significantly altered both in severe and mild COVID-19 patients and in the healthy adults in our study. *FOLR3* expression was down-regulated due to vitamin D supplementation in a dose-dependent manner (foldchange= $-1.0$ ,  $-1.7$ , and  $-2.7$  for the 600, 4,000, and 10,000 IU/day supplementation groups, respectively). As *FOLR3* is expressed in neutrophils as a secretory protein, a decreased *FOLR3* transcript level could indicate that vitamin D supplementation decreases neutrophil count as has been recently reported in patients admitted with severe symptoms. Patients who were vitamin D sufficient had a significant decrease in the number of neutrophils compared to lymphocytes. This could be a potential mechanism through which a higher vitamin D status reduces COVID-19 severity, as a high neutrophil count and neutrophil-lymphocyte ratio (NLR) are biomarkers for predicting severe health consequences from COVID-19.

## 19

OP No. 19

### IMPACT OF VITAMIN D IN ALZHEIMER'S DISEASE

Anna A. Lauer and Marcus O.W. Grimm

Experimental Neurology, Saarland University,  
Homburg (Saar), Germany

Alzheimer's disease (AD) is one of the most common neurodegenerative diseases affecting especially the older population. In the United States, it is estimated that over 500,000 new cases will be diagnosed this year. Several lines of evidence suggest a tight link between vitamin D hypovitaminosis and AD. However, very little is known about the molecular mechanisms linking AD with the vitamin D status. Utilizing neuroblastoma cells and a mouse model with mild vitamin D deficiency (20% reduction compared to wt mice) revealed that the secosteroid vitamin D affects several mechanisms involved in AD. Vitamin D affects directly the BACE gene expression and protein levels, which is in line with an altered BACE activity, leading to changed amyloid  $\beta$  ( $A\beta$ ) levels.  $A\beta$  is the major component of senile plaques, one of the characteristic pathological hallmarks of AD. Beside the  $A\beta$  anabolism, the catabolism is also affected by the vitamin D status, further emphasizing the crucial role of vitamin D in AD pathology. Similar effects have been found for vitamin  $D_2$  and  $D_3$

analogues. Furthermore, vitamin D regulates the expression of genes involved in oxidative stress (*Park7*), inflammation (*Casp4*), lipid metabolism (*AbcA1*), signal transduction (*Gnb5*), and neurogenesis (*Plat*) suggesting that vitamin D has not only a high impact on AD but also in other neurodegenerative diseases, which is also supported by current epidemiological studies.

## 20

OP No. 20

### SYNTHESIS OF $^{13}\text{C}$ -LABELLED VITAMIN D METABOLITES FOR THEIR USE IN LC-MS/MS APPLICATIONS

Lars Kattner

Endotherm Life Science Molecules, Saarbruecken,  
Germany

*Background/Aim:* Simultaneous assessment of various vitamin D metabolites in human biofluids by liquid chromatography-tandem mass spectrometry (LC-MS/MS) represents a new promising tool for the differential diagnosis of vitamin D-related diseases. Particularly, low-abundant medicinally-relevant vitamin D metabolites, such as  $25(\text{OH})\text{VD}_{2/3}$ ,  $24,25(\text{OH})_2\text{VD}_{2/3}$ ,  $1,25(\text{OH})_2\text{VD}_{2/3}$ , and  $1,24,25(\text{OH})_3\text{VD}_{2/3}$ , along with their 3-*epi*-derivatives have to be considered. *Materials and Methods:* The assessment of these metabolites requires the development of calibration and reference standards, that is, their labeling with multiple deuterium-, or even better,  $^{13}\text{C}$ - atoms. *Results:* Some  $^{13}\text{C}$ -labelled vitamin D metabolites have been chemically synthesized and obtained in good yield and high purity. *Conclusion:* Access to a wide variety of  $^{13}\text{C}$ -labelled highly pure vitamin D metabolites enables the advancement of LC-MS/MS applications towards a better understanding of differential diagnosis of vitamin D-related diseases.

## 21

OP No. 21

### EFFICACY OF VITAMIN $D_3$ SUPPLEMENTATION ON CANCER MORTALITY IN THE GENERAL POPULATION AND THE PROGNOSIS OF PATIENTS WITH CANCER: A SYSTEMATIC REVIEW AND INDIVIDUAL PATIENT DATA META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

Sabine Kuznia, Anna Zhu, Ben Schöttker and  
Hermann Brenner

Division of Clinical Epidemiology and Aging Research,  
German Cancer Research Center (DKFZ), Heidelberg,  
Germany