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OC.3-THE FIRST 2 YEARS OF EXPERIENCE OF THE TELETHON UNDIAGNOSED DISEASES PROGRAMS

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We present the experience of the first two years of the Telethon Undiagnosed Diseases Program (TUDP). TUDP is a national program founded by Fondazione Telethon aimed at the diagnosis of children with severe and multi-organ diseases that lack a genetic diagnosis. The aim of the program is to offer an accurate clinical re-evaluation of all patients and, if indicated, a Next Generation Sequencing (NGS) test. Most of those patients were already been visited by multiple centers and subject to invasive and non-invasive procedures. All were already tested with array-CGH. From April 2016 to June 2018, nine national pediatric centers have proposed 355 undiagnosed patients. Fifty-two have been considered as not eligible either because a diagnosis was already possible with patient data re-evaluation or the clinical manifestations were outside inclusion criteria. Of the 305 enrolled patients, 118 have completed the whole NGS analysis and results have been interpreted by comparison with medical literature and undiagnosed patient databases. Analysis of 54 patients (45%) has been positively concluded. Three patients had mutations in the same gene (DDXD3), two couples of patients in two genes (GRIN1 and ASXL3) and the rest of patients in single genes. Among these cases, 19 showed extension of the phenotypes already reported in literature and in one case a mutation in a new disease-gene was found. For unconcluded cases, 9 new candidate genes have been found with already matched second patients and follow-up studies are in progress.