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**Current Fields of Research**

The research is organized in teams that have close interaction. Included in the Unit are the headquarters of PRINTO and the Laboratory of Immunology of Rheumatic Diseases.

**Controlled clinical trials**

The unit is the headquarter of the Paediatric Rheumatology International Trials Organisation (PRINTO) ([www.printo.it](http://www.printo.it)). PRINTO, which was founded in 1996 by Alberto Martini and

Nicolino Ruperto, is composed by academic, clinical centres engaged in the care of children with paediatric rheumatic disease. It is composed of more than 200 centres from 51 countries and represents the largest paediatric rheumatology network in the world. PRINTO's main goal is to coordinate, foster and facilitate multi-centres, international controlled clinical trials. PRINTO has received 5 grants from the European Union and has published so far more than 70 papers. It has also developed a website dedicated to families ([www.pediatric-rheumatology.printo.it](http://www.pediatric-rheumatology.printo.it)) available in more than 50 languages and visited daily by more than 10,000 people.

### **Quantitative clinical assessment in paediatric rheumatic diseases**

This area of research is aimed to develop and validate new clinical measures for the assessment of disease activity, functional ability, clinical damage, pain, and health-related quality of life in children with paediatric rheumatic diseases. Some instruments put together different measures in a single multidimensional questionnaire that is aimed to assess all domains of disease impact simultaneously.

### **Imaging**

The aim is to provide standardized methods to evaluate the role of conventional radiology, magnetic resonance and ultrasonography in the evaluation of articular damage in juvenile idiopathic arthritis. The research of the unit has provided most of the available imaging scores to evaluate articular damage in children.

### **Immunology of rheumatic diseases**

The research is addressed at understanding the role of adaptive immunity in the pathogenesis of paediatric rheumatic diseases. Present research projects include the influence of innate immunity on the development of TH17 cells, the characterization of the immunological and functional phenotype of the different B cell populations and the role of TLRs and purinergic receptors during central and peripheral B cell development

### **Autoinflammatory diseases**

Starting from January 2002, a national referral center for the diagnosis and treatment of autoinflammatory diseases has been established. The Unit is the promoter of an European Union sponsored project (Eurofever) whose aim is to set up an international registry for autoinflammatory diseases. Laboratory activities are mainly focused on the pathogenesis of CIAS1-related diseases and of TNF-receptor-associated periodic syndrome (TRAPS).

### **Selected Publications**

1. Ruperto N, Lovell DJ, Quartier P, Paz E, Rubio-Pérez N, Silva CA, Abud-Mendoza C, Burgos-Vargas R, Gerloni V, Melo-Gomes JA, Saad-Magalhães C, Sztajn bok F, Goldenstein-Schainberg C, Scheinberg M, Calvo Penades I, Fischbach M, Orozco J, Hashkes PJ, Hom C, Jung L, Lepore L, Oliveira S, Wallace C, Sigal LH, Block AJ, Covucci A, Martini A, Giannini EH: Efficacy and safety of abatacept in children with juvenile idiopathic arthritis: a randomized, double-blind, placebo-controlled withdrawal trial. *Lancet* 2008; 372: 383–91  
IF: 28.638
2. Lovell DJ, Ruperto N, Goodman S, Reiff A, Jung L, Jarosova K, Nemcova D, Mouy R, Sandborg C, Bohnsack J, Elewaut D, Foeldvari I, Gerloni V, Rovensky J, Minden K, Vehe RK, Weiner LW, Horneff G, Huppertz H-I, Olson NY, Medich JR, Carcereri-De-Prati R, McIlraith MJ, Giannini EH, Martini A. A Randomized, Placebo-Controlled Trial of

Adalimumab with and without Methotrexate in Children with Polyarticular Juvenile Rheumatoid Arthritis. *N Engl J Med* 2008;339:810-820  
IF: 52.589

3. Ruperto N, Ozen S, Pistorio A, Dolezalova P, Brogan P, Cabral DA, Cuttica R, Khubchandani R, Lovell DJ, O'Neil KM, Quartier P, Ravelli A, Iusan SM, Filocamo GF, Saad Magalhães C, Unsal E, Oliveira S, Bracaglia C, Bagga A, Stanevicha V, Magni Manzoni S, Pratsidou P, Lepore L, Espada G, Kone Paut I, Zulian F, Barone P, Bircan Z, del Rocio Maldonado M, Russo R, Vilca I, Tullus K, Cimaz R, Horneff G, Anton J, Garay S, Nielsen S, Barbano G, Martini A. The EULAR/PRINTO/PRES criteria for Henoch-Schönlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis, and childhood Takayasu arteritis: ankara 2008. Part I: overall methodology and clinical characterisation. *Ann Rheum Dis* 2010;69:790-797  
IF: 8.111
4. Martini A, Lovell DJ. Juvenile idiopathic arthritis. State of the art and future perspectives *Ann Rheum Dis* 2010;69:1260-3  
IF: 8.111
5. Tassia S, Carta S, Delfino L, Caorsi R, Martini A, Gattorno M, Rubartelli A. Altered redox state of monocytes from cryopyrin-associated periodic syndromes causes accelerated IL-1beta secretion. *Proc Natl Acad Sci U S A* 2010;107:9789-94  
IF: 9.432
6. Vilca I, Garcia Munitis P, Pistorio A, Ravelli A, Buoncompagni A, Bica B, Campos L, Häfner R, Hofer M, Ozen S, Huemer C, Cheol Bae S, Sztajn bok F, Arguedas O, Foeldvari I, Huppertz HI, Gamir ML, Magnusson B, Dressler F, Uziel Y, van Rossum MAJ, Hollingworth P, Cawkwell G, Martini A, Ruperto N. Predictors of poor response to methotrexate in polyarticular-course juvenile idiopathic arthritis. analysis of the printo methotrexate trial. *Ann Rheum Dis* 2010;69:1479-83  
IF: 8.111
7. Schena F, Gambini C, Gregorio A, Mosconi M, Reverberi D, Gattorno M, Casazza S, Uccelli A, Moretta L, Martini A, Traggiai E. IFN-gamma dependent inhibition of B cell activation by bone marrow derived mesenchymal stem cells in a murine model of systemic lupus erythematosus. *Arthritis Rheum* 2010;62:2776-86  
IF: 7.332
8. Ruperto N, Giannini EH, Pistorio A, Brunner HI, Martini A, Lovell DJ. Is it time to move to active comparator trials in juvenile idiopathic arthritis?: a review of current study designs. *Arthritis Rheum.* 2010;62:3131-9.  
IF: 7.332
9. Malattia C, Damasio MB, Pistorio A, Ioseliani M, Vilca I, Valle M, Ruperto N, Viola S, Buoncompagni A, Magnano GM, Ravelli A, Tomà P, Martini A. Development and preliminary validation of a pediatric-targeted MRI scoring system for the assessment of disease activity and damage in juvenile idiopathic arthritis. *Ann Rheum Dis* 2010 Nov 24. [Epub ahead of print]  
IF: 8.111
10. Ravelli A, Varnier GC, Oliveira S, Castell E, Arguedas O, Magnani A, Pistorio A, Ruperto N, Magni-Manzoni S, Galasso R, Lattanzi B, Dalprà S, Battagliese A, Verazza S, Allegra M, Martini A. Antinuclear antibody positive patients should be grouped as a separate category in the classification of juvenile idiopathic arthritis. *Arthritis Rheum.* 2011;63:267-75.  
IF: 7.332

**Current Funding**

European Union  
Italian Agency of Drug Evaluation

**Training of Fellows in Research**

A dedicated fellowship training program for Italian and foreign physicians is in place. The program (from 3 months to 3 years) offers training in clinical management, clinical trials methodology, applied basic and intermediate biostatistics and epidemiology, and basic or clinical immunology. Since 2002 the unit has hosted 70 doctors from 23 countries. Fellows have been supported by public bodies (European Union and other) or self financed. A total of 11 EULAR training fellowships has been obtained since 2004.

**WebPages**

[www.printo.it](http://www.printo.it)

[www.pediatric-rheumatology.printo.it](http://www.pediatric-rheumatology.printo.it) (for families)

[www.gaslini.org](http://www.gaslini.org)