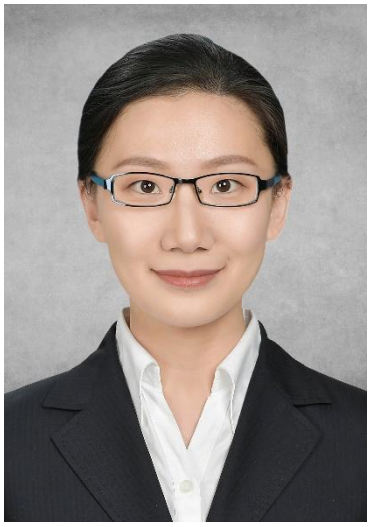
Year: 2023 **Type of Awards (Young)**

Name of Principal Investigator: Huichuan Qi **Affiliated Institution: Jilin University**

About of the PI



- **Introduction & Education:**

(Overview of your academic background and research focus, highlighting milestones of your journey as a researcher.)

Dr. Huichuan Qi received her Ph.D. in Orthodontics from Jilin University in collaboration with the University of California, Los Angeles in 2018 and finished her Orthodontics Residency Training at the Hospital of Stomatology, Jilin University in 2021. She completed her postdoctoral work at the School of Life Sciences, Jilin University from 2021 to 2023.

- **Career Trajectory:**

(Pivotal moments in your career, including positions held, significant projects, and notable achievements.)

Currently, Dr. Qi is an attending physician in the Department of Orthodontics, Hospital of Stomatology, Jilin University. With a strong interest in orthodontics, she mentors the residents and develops basic and clinical research. As a young teacher, she won first prize in the National Teaching Proficiency Competition for Young Teachers (Chinese Stomatological Association).

- **Research Contributions, Impact & Recognition:**

(Highlight major findings and contributions to your field, emphasizing the impact of your research.)

Dr. Qi's preliminary work advances the understanding of the chondrocyte-specific effects of Nell-1, and provides new molecular insight on its involvement in modulating cartilage homeostasis and endochondral ossification. Her study, published in the Journal of Bone and Mineral Research, Cell Death & Differentiation, etc., focuses on the growth, development, and remodeling of bone and cartilage tissues. She led several national and provincial projects and was honored as the Outstanding Young Researcher in Oral Biomedicine (Chinese Stomatological Association).

- **Personal Insights:**

(Offer insights into your personal interests, values, and motivations as a researcher, sharing anecdotes that have influenced your perspective.)

In view of the challenges to orthodontic treatment and suffering for patients caused by temporomandibular joint osteoarthritis (TMJOA), Dr. Qi started her study on modulating the homeostasis of mandibular condylar cartilage to provide a theoretical basis for the normal function maintenance of TMJ and the pathophysiology of TMJOA.

- **Future Directions:**

(Outline your envisioned research directions and aspirations, detailing how you plan to continue advancing knowledge and addressing emerging challenges in your field.)

The effects of Nell-1 on chondrocytes in response to mechanical loading will be explored as a potential research topic. Further studies on ion channels, primary cilia, and cytoskeleton to

probe the in-depth molecular mechanism of mechanosignal transduction in chondrocytes will be conducted.

Brief Summary of the Project:

The temporomandibular joint (TMJ), a synovial joint exposed to limited load-bearing forces, performs the most complicated movement in the human body. For orthodontists, the high prevalence and early onset of temporomandibular joint osteoarthritis (TMJOA) pose considerable challenges. TMJOA, characterized by progressive cartilage deterioration, has been identified as a consequence mainly arising from TMJ overload. As a novel osteochondrogenic factor, Nel-like molecule-1 (Nell-1) has been demonstrated to be essential for modulating epiphyseal homeostasis and inducing hyaline cartilage formation without mineralization or fibrosis. However, the role of Nell-1 in mandibular condylar cartilage remains unclear.

Our preliminary work showed an early onset of mouse osteoarthritic phenotype in Nell-1-deficient knee articular cartilage. Besides, Nell-1 was detected expressing in the mandibular condylar cartilage and increased under the condition of mandibular advancement. However, the gene and protein expression of Nell-1 was significantly decreased in response to overload. Furthermore, the Nell-1-knockdown ADTC5 cells showed reduced Col-2, increased MMP 13, enhanced Piezo1, and YAP nuclear translocation. Taken together, we hypothesize that Nell-1 is essential for maintaining the homeostasis of mandibular condylar cartilage.

In this study, we will assess the impact of Nell-1 deficiency on condylar cartilage using the newly generated Nell-1^{Acan}KO mice. Further exploration of Nell-1's functional role in maintaining the condylar cartilage homeostasis under mechanical loading will be conducted using the UAC mice and *in vitro* loading application to simulate malocclusion-induced TMJOA. Here, we propose a specific mode of action for Nell-1 in modulating the homeostasis of TMJ fibrocartilage, which will advance our understanding of the functional characteristics of Nell-1 and provide new insight on its involvement in converting mechanical stimuli into intercellular chemical signals.